EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	233	thalidomide.clm. and (cancer or tumor).clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/07/26 15:55
L2	0	l1 and @ad<"19930301"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/07/26 15:55
L3	1	thalidomide.clm. near4 (cancer or tumor).clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/07/26 15:56
L4	133	thalidomide near4 (cancer or tumor)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/07/26 16:00
L11	3445	thalidomide and (cancer or tumor)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/07/26 16:06
L12	52	l11 and "d'amato".in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/07/26 16:01
L13	14	thalidomide.clm. and (cancer or tumor) and d'amato.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/07/26 16:02
L14	0	l11 and @ad<"1993"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/07/26 16:07

EAST Search History

L15	0	l11 and @ad<="1993"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/07/26 16:07
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L17	0	l1 and @ad<="19930301"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/07/26 16:08

09/704,054

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FILE 'HOME' ENTERED AT 15:35:25 ON 26 JUL 2007

=> FIL REGISTRY
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.42       0.42

FILE 'REGISTRY' ENTERED AT 15:36:20 ON 26 JUL 2007
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STRUCTURE FILE UPDATES:   25 JUL 2007  HIGHEST RN 943407-83-8
DICTIONARY FILE UPDATES:  25 JUL 2007  HIGHEST RN 943407-83-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> E "THALIDOMIDE"/CN 25
E1             1     THALIDICINE/CN
E2             1     THALIDINE/CN
E3             1 --> THALIDOMIDE/CN
E4             1     THALIDOMIDE-ASPIRIN MIXT./CN
E5             1     THALIDOMIDE-INDOMETHACIN MIXT./CN
E6             1     THALIDOMIDE-PREDNISOLONE MIXT./CN
E7             1     THALIDOMIDE-PREDNISONE MIXT./CN
E8             1     THALIDOXINE/CN
E9             1     THALIDOXINE ACETATE/CN
E10            1     THALIFABATINE/CN
E11            1     THALIFABERIDINE/CN
E12            1     THALIFABERINE/CN
E13            1     THALIFABINE/CN
E14            1     THALIFABOMINE/CN
E15            1     THALIFABORAMINE/CN
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E22            1     THALIFAROLINE/CN
E23            1     THALIFARONINE/CN
E24            1     THALIFASINE/CN
E25            1     THALIFASINE DIACETATE/CN
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=> S E3
L1              1 THALIDOMIDE/CN

=> DIS L1 1 SQIDE
THE ESTIMATED COST FOR THIS REQUEST IS 6.55 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L1    ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN    50-35-1  REGISTRY
CN    1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)-   (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN    Phthalimide, N-(2,6-dioxo-3-piperidyl)- (6CI, 7CI, 8CI)
OTHER NAMES:
CN    (±)-Thalidomide
CN    α-(N-Phthalimido)glutarimide
CN    α-N-Phthalylglutaramide
CN    α-Phthalimidoglutarimide
CN    1,3-Dioxo-2-(2,6-dioxopiperidin-3-yl)isoindoline
CN    3-Phthalimidoglutarimide
CN    Celgene
CN    Contergan
CN    Distaval
CN    K 17
CN    Kevadon
CN    Myrin
CN    N-(2,6-Dioxo-3-piperidyl)phthalimide
CN    N-Phthaloylglutamimide
CN    Neurosedyn
CN    NSC 527179
CN    NSC 66847
CN    Pantosediv
CN    Quetimid
CN    Sauramide
CN    Sedalis
CN    Sedoval
CN    Softenil
CN    Softenon
CN    Suaramide
CN    Talimol
CN    Talinol
CN    Thalidomide
CN    Thalomid
DR    14088-68-7, 731-40-8
MF    C13 H10 N2 O4
CI    COM
LC    STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*,
        BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS,
        CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, HSDB*, IMSCOSEARCH,
        IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS,
        PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER,
        USAN, USPAT2, USPATFULL
          (*File contains numerically searchable property data)
      Other Sources:   EINECS**, WHO
          (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type:  Book; Conference; Dissertation; Journal; Patent;
      Report
RL.P  Roles from patents:  ANST (Analytical study); BIOL (Biological study);
      PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
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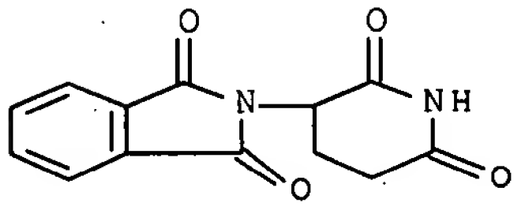
reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2582 REFERENCES IN FILE CA (1907 TO DATE)
163 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2595 REFERENCES IN FILE CAPLUS (1907 TO DATE)
15 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> file medline caplus wpids uspatfull

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.80	8.22

FILE 'MEDLINE' ENTERED AT 15:37:30 ON 26 JUL 2007

FILE 'CAPLUS' ENTERED AT 15:37:30 ON 26 JUL 2007
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FILE 'WPIDS' ENTERED AT 15:37:30 ON 26 JUL 2007

FILE 'USPATFULL' ENTERED AT 15:37:30 ON 26 JUL 2007

=> s l1
L2 6948 L1

=> s l2 and (cancer or tumor or tumorogenesis)
L3 2153 L2 AND (CANCER OR TUMOR OR TUMOROGENESIS)

=> s l3 not py>1995
L4 109 L3 NOT PY>1995

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=> s l4 not py>1993
L5            63 L4 NOT PY>1993

=> s l5 and angiogenesis
L6             0 L5 AND ANGIOGENESIS

=> s l5 and "tumor growth"
L7             6 L5 AND "TUMOR GROWTH"

=> d l7 1-6 ibib abs hitstr

L7   ANSWER 1 OF 6      MEDLINE on STN
ACCESSION NUMBER:    67045840      MEDLINE  Full-text
DOCUMENT NUMBER:     PubMed ID: 5924955
TITLE:               Effect of various agents on liver regeneration and Walker
                     tumor growth in partially hepatectomized
                     rats.
AUTHOR:              Gershbein L L
SOURCE:              Cancer research, (1966 Sep) Vol. 26, No. 9, pp. 1905-8.
                     Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         196702
ENTRY DATE:          Entered STN: 1 Jan 1990
                     Last Updated on STN: 1 Jan 1990
                     Entered Medline: 5 Feb 1967

L7   ANSWER 2 OF 6  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        1976:537359  CAPLUS  Full-text
DOCUMENT NUMBER:         85:137359
TITLE:                   Factors related to tumor spread in the body
AUTHOR(S):               Boggust, W. A.
CORPORATE SOURCE:        Dep. Exp. Med., Trinity Coll., Dublin, Ire.
SOURCE:                  Advances in Tumour Prevention, Detection and
                         Characterization (1976), 3(Biol. Charact. Hum.
                         Tumours, Proc. Int. Symp., 6th, 1975), 383-90
                         CODEN: APDCDT
DOCUMENT TYPE:           Journal
LANGUAGE:                English
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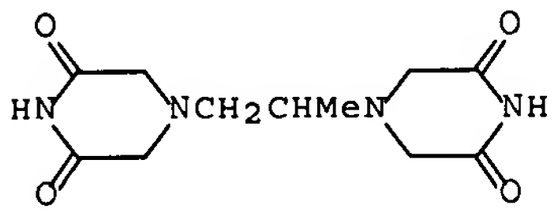
GI



II

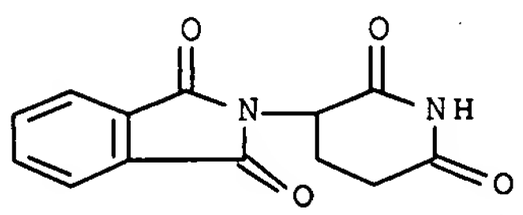
AB In exts. of human cancers, cathepsins B, C, and D, leucine aminopeptidase [9001-61-0], glucosaminidase [9027-56-9], acid and neutral collagenase [9001-12-1], and fibrinolysin [9001-90-5] activities were found. Collagenase was blocked by the chelating agents dimercaptopropanol (BAL) [59-52-9], EDTA [60-00-4], and o-phenanthroline (I) [66-71-7], and the cytostatic drug ICRF-159

(II) [21416-87-5]. Combinations of I and II were synergistic. II also inhibited cathepsins C and B1 and probably glucosaminidase, but not cathepsin D or leucineaminopeptidase. Mice bearing implanted carcinoma excised on the 10th day, died from lung metastases within 34 days unless otherwise treated. Survival periods were increased by II, but not by I alone. Combinations of I and II substantially increased the survival period. Thus, I and II by acting as enzyme inhibitors and cytotoxic agents they helped to inhibit primary tumor growth and prevent metastases.

IT 50-35-1
RL: BIOL (Biological study)
(enzymes inhibition by, in neoplasm)

RN 50-35-1 CAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (CA INDEX NAME)



L7 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1966:501712 CAPLUS Full-text

DOCUMENT NUMBER: 65:101712

ORIGINAL REFERENCE NO.: 65:19035g-h,19036a-b

TITLE: Stimulation of growth by subliminal concentrations of growth-inhibiting substances

AUTHOR(S): Rauen, H. M.; Norpoth, K.

CORPORATE SOURCE: Univ. Muenster, Germany

SOURCE: Arzneimittel-Forschung (1966), 16(8), 1001-7
CODEN: ARZNAD; ISSN: 0004-4172

DOCUMENT TYPE: Journal

LANGUAGE: German

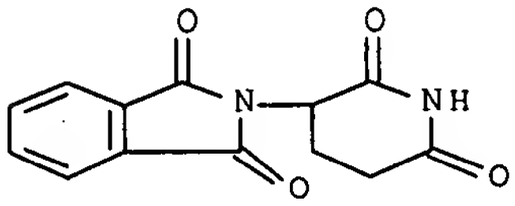
AB 2-Amino-4,6-dimethylpyrimidine at 50-200 γ/ml. stimulated growth of Neurospora crassa, but at higher concns., it was inhibitory. 4,5-Diamino-1,3-dimethyl-2,6-dihydroxypyrimidine at 10-50 γ/ml. stimulated N. crassa growth, but at 200-2000 γ/ml. inhibited it. 2-Amino-4-chloropyrimidine and 2-amino4-chloro-6-methylpyrimidine produced similar results. Actinomycin D (1-3 γ/ml.) stimulated growth of Sordaria macrospora, but at 5 γ/ml. inhibited growth. Thalidomide (≤200 γ/ml.). stimulated growth of Lactobacillus fermenti, 500-1000 γ/ml. inhibited growth. N,N-Bis(2-chloroethyl)-N',O- propylenephosphoric acid ester diamide and bis-(β-chloroethyl)amine- HCl at low concns. stimulated growth of yeasts, lactobacilli, and Escherichia coli, but inhibited growth at high concns. The coplanar heterooligobases, HR-1887, HR-2257, and HR-2074, shifted the growth curve of Streptomyces faecalis R to the right. Sandoz SP-G (which contains podophyllotoxin β-D-benzylidene glucoside, 4'-demethylpodophyllotoxin β-D-benzylidene glucoside, and some other natural compds.), derived from rhizomes of Podophyllure emodi, did not inhibit 2 strains of Micrococcus pyrogenes, E. coli, Proteus vulgaris, Saccharomyces cerevisiae, or Amoeba proteus; it slightly inhibited L. casei, L. arabinosus, L. mesenteroides, and Bacillus cereus; but it greatly inhibited growth of L. fermenti and stimulated growth of S. faecalis. Sandoz SP-I (podophyllic acid ethyl hydrazide) had a much weaker effect on L. fermenti, but a similar effect on L. casei and B. cereus compared with Sandoz SP-G. Sandoz SP-I did not

influence growth of S. faecalis, L. arabinosus or L. mesenteroides. Growth of Jensen sarcoma transplanted on the chorioallantois of hatched hen eggs was stimulated by 20 γ of HR-2074/egg and was inhibited by 500 γ to 1 mg./egg. Sandoz SP-G (100 γ/egg) stimulated the growth of transplanted Voshida sarcoma, whereas 1 mg./egg inhibited growth. Sandoz SP-I produced similar results with Jensens sarcoma and Walker carcinosarcoma. Verrucarin A isolated from Myrothecium verrucaria and anguidin at 1 mg./egg inhibited growth of Yoshida sarcoma but stimulated growth of DS-carcinosarcoma. Low doses of cytostatics can stimulate microbial and tumor growth. 29 references.

IT 50-35-1P, Phthalimide, N-(2,6-dioxo-3-piperidyl)-
RL: PREP (Preparation)
(Lactobacillus fermenti stimulation by subliminal concentration of)

RN 50-35-1 CAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (CA INDEX NAME)



L7 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1966:493663 CAPLUS Full-text

DOCUMENT NUMBER: 65:93663

ORIGINAL REFERENCE NO.: 65:17554c-e

TITLE: Effect of various agents on liver regeneration and Walker tumor growth in partially hepatectomized rats

AUTHOR(S): Gershbein, Leon L.

CORPORATE SOURCE: Northwest Inst. for Med. Res., Chicago

SOURCE: Cancer Research (1966), 26(9;Pt. 1), 1905-8
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

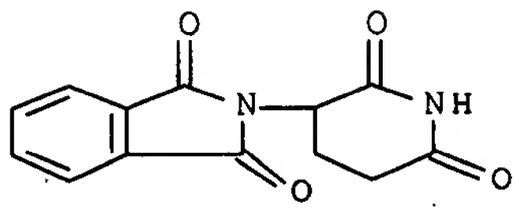
LANGUAGE: English

AB The restoration of liver weight in subtotally hepatectomized rats with Walker tumor cells transplanted into the caudal lobe of the remaining liver, was stimulated by feeding diets supplemented with coramine, butazolidine, 2,4-dithiopyrimidine, thalidomide, and acenaphthene, or by subcutaneous injections of acenaphthene, or 9,10-dimethyl-1,2- benzanthracene. Thiouracil, disulfiram, and usnic acid gave rise to liver weight increments which were in the range of their resp. controls. Dietary supplements of nicotinamide, cycloleucine, D-Lethionine, and 6-mercaptopurine, or a subcutaneous injection of cortisone acetate decreased the liver weight gain to levels below that of their resp. controls. The mean wet tumor wts. were not affected by any of these drugs, except by nicotinamide, which elicited a decrease in tumor weight 18 references.

IT 50-35-1P, Phthalimide, N-(2,6-dioxo-3-piperidyl)-
RL: PREP (Preparation)
(in liver regeneration and neoplasm growth after partial hepatectomy)

RN 50-35-1 CAPLUS

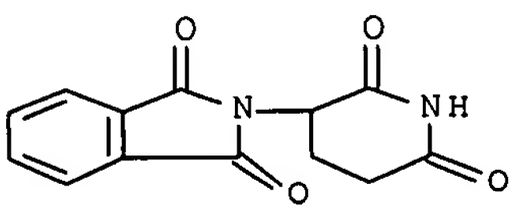
CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (CA INDEX NAME)



L7 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:30357 CAPLUS Full-text
DOCUMENT NUMBER: 64:30357
ORIGINAL REFERENCE NO.: 64:5658d-f
TITLE: Biochemical effects of thalidomide and a histogenetic hypothesis of the malformation of the fetus
AUTHOR(S): Nystrom, Cl.
CORPORATE SOURCE: Univ. Sahlgrenska Sjukhuset, Goteborg, Swed.
SOURCE: Intern. Congr. Chemotherapy, Proc., 3rd, Stuttgart (1964), 1963(1), 372-8
DOCUMENT TYPE: Journal
LANGUAGE: English

AB cf. CA 59, 4441g. Since thalidomide (I) has an N-phthaloylglutamic acid imide structure its possible actions as an antimetabolite against folic acid (II) was investigated. Over 1-3 months, I was administered by injection and orally to 2 patients with tetratoid carcinomas of an embryonal type, presumably with enzyme patterns like that of a fetus. One was a woman of 25 years with an ovarian cancer, the other was a man of 42 with carcinoma of the testes. Blood levels of II were little affected by I. However, I had some effect as an antagonist to II. In doses higher than 3 g./day (as high as 7 g./day), I appeared to interfere with II metabolism as indicated by increased amts. of urinary formiminoglutamic acid. In growth inhibition tests, I did not affect the growth of Streptococcus faecalis or Lactobacillus casei. Hence I did not act as a II antagonist in bacterial growth. For the in vivo human tests, there was an uptake of I by tumor tissue but no particularly marked effects of I on tumor growth. This may perhaps have resulted from the fact that the tumors and their metastases had been treated with heavy doses of ionizing radiations. However, the results suggested that II-dependent tumors might show pharmacotherapeutic responses to I or some of its metabolites. 13 references.

IT 50-35-1P, Phthalimide, N-(2,6-dioxo-3-piperidyl)-
RL: PREP (Preparation)
(preparation of)
RN 50-35-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (CA INDEX NAME)



L7 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:406964 CAPLUS Full-text

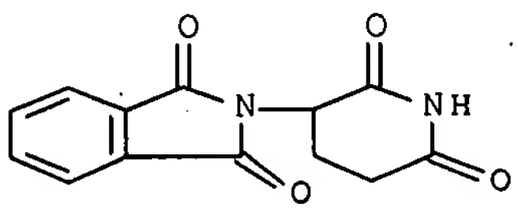
DOCUMENT NUMBER: 61:6964
ORIGINAL REFERENCE NO.: 61:1130f
TITLE: The possible antineoplastic effect of thalidomide
AUTHOR(S): Bach, A.; Bichel, J.; Hejgaard, J. J.
CORPORATE SOURCE: Union Aarhus, Den.
SOURCE: Acta Pathologica et Microbiologica Scandinavica (1963), 59(4), 491-9
CODEN: APMIAL; ISSN: 0365-5555
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mice were relatively insensitive to thalidomide, and even doses many times larger than those which are definitely hypnotic in man did not produce any visible sedative effect. Amts. 1000 times as high as the hypnotic dose/kg. body weight in man induced sleep for some hours in the animals, which could, however, always easily be aroused. Very large doses of thalidomide did not show any inhibitory effect on NJA, PBH, and GH tumor growth in C3H mice.

IT 50-35-1, Phthalimide, N-(2,6-dioxo-3-piperidyl)-
(neoplasm response to)

RN 50-35-1 CAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 15:35:25 ON 26 JUL 2007)

FILE 'REGISTRY' ENTERED AT 15:36:20 ON 26 JUL 2007
E "THALIDOMIDE"/CN 25
L1 1 S E3

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 15:37:30 ON 26 JUL 2007
L2 6948 S L1
L3 2153 S L2 AND (CANCER OR TUMOR OR TUMOROGENESIS)
L4 109 S L3 NOT PY>1995
L5 63 S L4 NOT PY>1993
L6 0 S L5 AND ANGIOGENESIS
L7 6 S L5 AND "TUMOR GROWTH"

=> s l5 and "tumor"
L8 53 L5 AND "TUMOR"

=> d l5 1-63 ibib abs

L5 ANSWER 1 OF 63 MEDLINE on STN
ACCESSION NUMBER: 94232213 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8177242
TITLE: Inhibition of tumor necrosis factor-alpha by thalidomide in magnesium deficiency.

AUTHOR: Weglicki W B; Stafford R E; Dickens B F; Mak I T; Cassidy M M; Phillips T M
CORPORATE SOURCE: Department of Medicine, George Washington University Medical Center, Washington, DC 20037.
CONTRACT NUMBER: P01-HL-38079 (NHLBI)
R01-49232
SOURCE: Molecular and cellular biochemistry, (1993 Dec 22) Vol. 129, No. 2, pp. 195-200.
Journal code: 0364456. ISSN: 0300-8177.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 20 Jun 1994
Last Updated on STN: 20 Jun 1994
Entered Medline: 7 Jun 1994

AB The effect of thalidomide on circulating cytokines and myocardial lesion formation was investigated in Mg-deficient rats. After two weeks on a Mg-deficient diet, rats show an increase in circulating levels of tumor necrosis factor-alpha and interleukin 1. Thalidomide (1 mg/day) caused a complete inhibition of the increase in circulating tumor necrosis factor-alpha levels, without having an effect on interleukin 1. However, a marked increase in cardiomyopathic lesion formation was observed in Mg-deficient animals treated with thalidomide; possible mechanisms for thalidomide's enhancement of myocardial injury are discussed.

L5 ANSWER 2 OF 63 MEDLINE on STN
ACCESSION NUMBER: 93360618 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8355553
TITLE: [Treatment with thalidomide and production of tumor necrosis factor alpha].
Terapeutica con talidomida y produccion del factor de necrosis tumoral alfa.
AUTHOR: Pizarro A; Pinilla J; Garcia-Tobaruela A
SOURCE: Medicina clinica, (1993 Jun 19) Vol. 101, No. 4, pp. 158.
Journal code: 0376377. ISSN: 0025-7753.
PUB. COUNTRY: Spain
DOCUMENT TYPE: Commentary
Letter
LANGUAGE: Spanish
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 8 Oct 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 17 Sep 1993

L5 ANSWER 3 OF 63 MEDLINE on STN
ACCESSION NUMBER: 93329195 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8335978
TITLE: The influence of thalidomide on the clinical and immunologic manifestation of erythema nodosum leprosum.
AUTHOR: Sampaio E P; Kaplan G; Miranda A; Nery J A; Miguel C P; Viana S M; Sarno E N
CORPORATE SOURCE: Leprosy Unit, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil.
CONTRACT NUMBER: AI-22616 (NIAID)
SOURCE: The Journal of infectious diseases, (1993 Aug) Vol. 168,

No. 2, pp. 408-14.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 3 Sep 1993
Last Updated on STN: 3 Sep 1993
Entered Medline: 24 Aug 1993

AB Immunologic and clinical manifestations of erythema nodosum leprosum (ENL) and their response to thalidomide therapy were evaluated. Circulating tumor necrosis factor-alpha (TNF alpha) levels were assayed in serum obtained from lepromatous leprosy patients at diagnosis, during multidrug therapy, at the onset of ENL episodes, and during treatment with thalidomide. Patients with systemic ENL demonstrated the highest serum TNF alpha levels, which decreased significantly during thalidomide treatment. Serum TNF alpha in nonreactional patients was associated with mild flu-like symptoms and local inflammatory lesions. Serum interferon-gamma (IFN-gamma) was also elevated in patients with high TNF alpha levels. Thalidomide therapy reduced not only serum TNF alpha levels and the clinical symptoms but also the dermal infiltration of polymorphonuclear leukocytes and T cells. The expression of intercellular adhesion molecule 1 and major histocompatibility complex class II antigens on the epidermal keratinocytes was also down-regulated. These results indicate that the thalidomide-induced alleviation of clinical symptoms of ENL was associated with a reduction of TNF alpha levels.

L5 ANSWER 4 OF 63 MEDLINE on STN
ACCESSION NUMBER: 93317606 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8327469
TITLE: Thalidomide inhibits the replication of human immunodeficiency virus type 1.
AUTHOR: Makonkawkeyoon S; Limson-Pobre R N; Moreira A L; Schauf V; Kaplan G
CORPORATE SOURCE: Rockefeller University, New York, NY 10021.
CONTRACT NUMBER: AI-22616 (NIAID)
AI-24775 (NIAID)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1993 Jul 1) Vol. 90, No. 13, pp. 5974-8.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 20 Aug 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 6 Aug 1993

AB Thalidomide, a selective inhibitor of tumor necrosis factor alpha (TNF-alpha) synthesis, suppresses the activation of latent human immunodeficiency virus type 1 (HIV-1) in a monocytoid (U1) line. The inhibition is dose dependent and occurs after exposure of the cells to recombinant TNF-alpha, phorbol myristate acetate, lipopolysaccharide, and other cytokine combinations. Associated with HIV-1 inhibition is a reduction in agonist-induced TNF-alpha

protein and mRNA production. Thalidomide inhibition of virus replication in the phorbol myristate acetate- and recombinant TNF-alpha-stimulated T-cell line ACH-2 is not observed. The presence of thalidomide also inhibits the activation of virus in the peripheral blood mononuclear cells of 16 out of 17 patients with advanced HIV-1 infection and AIDS. These results suggest the use of thalidomide in a clinical setting to inhibit both virus replication and the TNF-alpha-induced systemic toxicity of HIV-1 and opportunistic infections.

L5 ANSWER 5 OF 63 MEDLINE on STN
ACCESSION NUMBER: 93267219 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8496685
TITLE: Thalidomide exerts its inhibitory action on tumor necrosis factor alpha by enhancing mRNA degradation.
AUTHOR: Moreira A L; Sampaio E P; Zmuidzinas A; Frindt P; Smith K A; Kaplan G
CORPORATE SOURCE: Laboratory of Cellular Physiology and Immunology, Rockefeller University, New York, New York 10021.
CONTRACT NUMBER: AI-22616 (NIAID)
AI-33124 (NIAID)
SOURCE: The Journal of experimental medicine, (1993 Jun 1) Vol. 177, No. 6, pp. 1675-80.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199306
ENTRY DATE: Entered STN: 2 Jul 1993
Last Updated on STN: 2 Jul 1993
Entered Medline: 21 Jun 1993

AB We have examined the mechanism of thalidomide inhibition of lipopolysaccharide (LPS)-induced tumor necrosis factor alpha (TNF-alpha) production and found that the drug enhances the degradation of TNF-alpha mRNA. Thus, the half-life of the molecule was reduced from approximately 30 to approximately 17 min in the presence of 50 micrograms/ml of thalidomide. Inhibition of TNF-alpha production was selective, as other LPS-induced monocyte cytokines were unaffected. Pentoxifylline and dexamethasone, two other inhibitors of TNF-alpha production, are known to exert their effects by means of different mechanisms, suggesting that the three agents inhibit TNF-alpha synthesis at distinct points of the cytokine biosynthetic pathway. These observations provide an explanation for the synergistic effects of these drugs. The selective inhibition of TNF-alpha production makes thalidomide an ideal candidate for the treatment of inflammatory conditions where TNF-alpha-induced toxicities are observed and where immunity must remain intact.

L5 ANSWER 6 OF 63 MEDLINE on STN
ACCESSION NUMBER: 93103729 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1466907
TITLE: Effect of blocking TNF-alpha on intracellular BCG (Bacillus Calmette Guerin) growth in human monocyte-derived macrophages.
AUTHOR: Fazal N; Lammas D A; Raykundalia C; Bartlett R; Kumararatne D S
CORPORATE SOURCE: Department of Immunology, University of Birmingham, UK.
SOURCE: FEMS microbiology immunology, (1992 Dec) Vol. 5, No. 5-6, pp. 337-45.

Journal code: 8901230. ISSN: 0920-8534.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199301
ENTRY DATE: Entered STN: 12 Feb 1993
Last Updated on STN: 12 Feb 1993
Entered Medline: 25 Jan 1993

AB Four agents, thalidomide, oxpentifylline, dexamethasone and a polyclonal anti-TNF-alpha antibody, were all shown by specific Elisa to block endogenous TNF-alpha production by Bacillus Calmette Guerin (BCG)-infected human monocyte-derived macrophages in in vitro culture. There was however no significant enhancement of intracellular BCG growth, over a 7-day incubation, in human monocyte-derived macrophages in the presence of any of the TNF-alpha-blocking agents, as determined by both radiometric and CFU counting methods of assessing bacterial viability and growth. The result suggests that the action of TNF-alpha alone is unlikely to be an important effector mechanism in antimycobacterial immunity within human cells.

L5 ANSWER 7 OF 63 MEDLINE on STN
ACCESSION NUMBER: 92268822 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1588290
TITLE: Prolonged treatment with recombinant interferon gamma induces erythema nodosum leprosum in lepromatous leprosy patients.
AUTHOR: Sampaio E P; Moreira A L; Sarno E N; Malta A M; Kaplan G
CORPORATE SOURCE: Laboratory of Cellular Physiology and Immunology, Rockefeller University, New York, New York 10021.
CONTRACT NUMBER: AI-22616 (NIAID)
SOURCE: The Journal of experimental medicine, (1992 Jun 1) Vol. 175, No. 6, pp. 1729-37.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 10 Jul 1992
Last Updated on STN: 10 Jul 1992
Entered Medline: 23 Jun 1992

AB 10 patients with borderline and lepromatous leprosy were selected for a prolonged trial with recombinant interferon gamma (rIFN-gamma). Patients received 30 micrograms intradermally for six injections over a 9-d period, and then either 100 micrograms intradermally every 1 mo for 10 mo or every 2 wk for 5 mo (total, 1.2 mg). Erythema nodosum leprosum (ENL) was induced in 60% of the patients within 6-7 mo, as compared with an incidence of 15% per year with multiple drug therapy alone. The mean whole-body reduction in bacterial index over the first 6 mo was 0.9 log units. Cutaneous induration at the intradermal injection sites of greater than or equal to 15 mm predicted the development of a subsequent reactional state. Monocytes obtained from patients receiving the lymphokine demonstrated an increased respiratory burst and a 2.5-5.1-fold increase in tumor necrosis factor alpha (TNF-alpha) secretion in response to agonists. Patients in ENL had an even higher release of TNF-alpha from monocytes as well as high levels of TNF-alpha in the plasma (mean, 2,000 pg/ml). Thalidomide therapy was required to treat the systemic

manifestations of ENL. Control of toxic symptoms with thalidomide was associated with a 50-80% reduction in agonist-stimulated monocyte TNF-alpha secretion. IFN-gamma enhanced the monocyte release of TNF-alpha by 3-7.5-fold (agonist dependent) when added to patient's cells in vitro, and this could be suppressed by the in vitro addition of 10 micrograms/ml of thalidomide.

L5 ANSWER 8 OF 63 MEDLINE on STN
ACCESSION NUMBER: 92195361 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1549151
TITLE: Thalidomide for the treatment of chronic graft-versus-host disease.
AUTHOR: Vogelsang G B; Farmer E R; Hess A D; Altamonte V; Beschorner W E; Jabs D A; Corio R L; Levin L S; Colvin O M; Wingard J R; +
CORPORATE SOURCE: Department of Oncology, Johns Hopkins University School of Medicine, Baltimore, Md.
CONTRACT NUMBER: CA-15396 (NCI)
R01-CA-44783 (NCI)
SOURCE: The New England journal of medicine, (1992 Apr 16) Vol. 326, No. 16, pp. 1055-8.
Journal code: 0255562. ISSN: 0028-4793.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 9 May 1992
Last Updated on STN: 9 May 1992
Entered Medline: 21 Apr 1992

AB BACKGROUND. Allogeneic bone marrow transplantation is an accepted therapy for hematologic cancer, aplastic anemia, and inherited immunodeficiencies. Chronic graft-versus-host disease (GVHD) is the principal complication in patients surviving more than 100 days. Thalidomide has been shown experimentally to be effective in treating GVHD. METHODS. We treated 23 patients with chronic GVHD refractory to conventional treatment and 21 patients with "high-risk" chronic GVHD (identified as having at least two of the following three risk factors: chronic GVHD that has evolved from acute GVHD, lichenoid skin or mucous-membrane changes, and hepatic dysfunction. Such patients have a high mortality rate.) with thalidomide in a dose that produced a plasma level of 5 micrograms per milliliter two hours after administration. Therapy was continued for three months after a complete response or for six months after a partial response. RESULTS. The overall actuarial survival of all enrolled patients was 64 percent. Survival was 76 percent among the patients receiving salvage therapy for refractory GVHD and 48 percent among those with high-risk GVHD. A complete response was observed in 14 patients, a partial response in 12 patients, and no response in 18. Side effects were minor, most notably sedation in almost all patients. CONCLUSIONS. In this preliminary trial, thalidomide appeared to be safe and effective for the treatment of chronic GVHD. A trial comparing thalidomide with prednisone in patients with newly diagnosed chronic GVHD will be required to demonstrate its relative efficacy.

L5 ANSWER 9 OF 63 MEDLINE on STN
ACCESSION NUMBER: 91203215 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2016904

TITLE: Induction of morphological differentiation in the human leukemic cell line K562 by exposure to thalidomide metabolites.
AUTHOR: Hatfill S J; Fester E D; de Beer D P; Bohm L
CORPORATE SOURCE: Radiotherapy Department, Faculty of Medicine, University of Stellenbosch, Tygerberg, R.S.A.
SOURCE: Leukemia research, (1991) Vol. 15, No. 2-3, pp. 129-36.
Journal code: 7706787. ISSN: 0145-2126.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 7 Jun 1991
Last Updated on STN: 3 Feb 1997
Entered Medline: 17 May 1991

AB The lineage and state of differentiation of cells in the mammalian haemopoietic compartment is associated with specific patterns of homeobox gene expression (EMBO J. 7, 2131, 1988). Agents which influence homeobox gene expression are thus of great interest in the study of human leukemias. Retinoic acid has direct regulatory actions on homeobox gene transcription (TIBS 158, 52, 1989; Differentiation 37, 773, 1988) and can induce select human leukemia cell lines to undergo terminal differentiation in vitro (Proc. natl Acad. Sci. U.S.A. 77, 2936, 1980). Retinoic acid is also a known teratogen for vertebrate foetal limb-bud development. Some of the teratogenic effects are duplicated by the drug Thalidomide (Embryopathic Activity of Drugs, Little Brown, Boston, p. 167, 1965; Haematological Cytology, Wolf Med. Pub. Ltd, London, p. 118, 1982). To investigate Thalidomide for other retinoid-like effects, we exposed cultures of human leukemia K562 cells to the metabolites generated in a Thalidomide hepatic-microsomal enzyme drug metabolizing system (Proc. natl Acad. Sci. U.S.A. 78, 2545, 1981). Here we report evidence that a single 2 h pulse-exposure to Thalidomide metabolites, induces K562 cells to undergo morphological differentiation in vitro. We also demonstrate a significant cytotoxic effect for these metabolites.

L5 ANSWER 10 OF 63 MEDLINE on STN
ACCESSION NUMBER: 91147899 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1997652
TITLE: Thalidomide selectively inhibits tumor necrosis factor alpha production by stimulated human monocytes.
AUTHOR: Sampaio E P; Sarno E N; Galilly R; Cohn Z A; Kaplan G
CORPORATE SOURCE: Laboratory of Cellular Physiology and Immunology, Rockefeller University, New York, New York 10021.
CONTRACT NUMBER: AI-22616 (NIAID)
SOURCE: The Journal of experimental medicine, (1991 Mar 1) Vol. 173, No. 3, pp. 699-703.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199104
ENTRY DATE: Entered STN: 19 Apr 1991
Last Updated on STN: 3 Feb 1997
Entered Medline: 2 Apr 1991

AB Thalidomide selectively inhibits the production of human monocyte tumor necrosis factor alpha (TNF-alpha) when these cells are triggered with lipopolysaccharide and other agonists in culture. 40% inhibition occurs at the clinically achievable dose of the drug of 1 micrograms/ml. In contrast, the amount of total protein and individual proteins labeled with [35S]methionine and expressed on SDS-PAGE are not influenced. The amounts of interleukin 1 beta (IL-1 beta), IL-6, and granulocyte/macrophage colony-stimulating factor produced by monocytes remain unaltered. The selectivity of this drug may be useful in determining the role of TNF-alpha in vivo and modulating its toxic effects in a clinical setting.

L5 ANSWER 11 OF 63 MEDLINE on STN
ACCESSION NUMBER: 86123775 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 3945939
TITLE: Teratogen metabolism: thalidomide activation is mediated by cytochrome P-450.
AUTHOR: Braun A G; Harding F A; Weinreb S L
SOURCE: Toxicology and applied pharmacology, (1986 Jan) Vol. 82, No. 1, pp. 175-9.
Journal code: 0416575. ISSN: 0041-008X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 198603
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 21 Mar 1990
Entered Medline: 4 Mar 1986

AB A metabolite of thalidomide generated by hepatic microsomes inhibited the attachment of tumor cells to concanavalin A-coated polyethylene. Evidence that metabolite formation is mediated by microsomal cytochrome P-450 is presented. Microsomes incubated with thalidomide underwent a type I spectral shift. Metabolite formation was reduced or eliminated by carbon monoxide, SKF-525A, metyrapone, and N-octylamine. Superoxide dismutase treatment had no effect. Metabolite formation required microsomes and NADPH and was dependent on the length of 37 degrees C incubation. The metabolite could be isolated by successive hexane and chloroform extractions. It is likely the inhibitory thalidomide metabolite was generated by a minor cytochrome P-450 species. Whether this thalidomide metabolite is involved in the drug's teratogenic activity remains to be shown.

L5 ANSWER 12 OF 63 MEDLINE on STN
ACCESSION NUMBER: 86071093 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2866599
TITLE: Teratogen metabolism: spontaneous decay products of thalidomide and thalidomide analogues are not bioactivated by liver microsomes.
AUTHOR: Braun A G; Weinreb S L
SOURCE: Teratogenesis, carcinogenesis, and mutagenesis, (1985) Vol. 5, No. 3, pp. 149-58.
Journal code: 8100917. ISSN: 0270-3211.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS

ENTRY MONTH: 198601
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 21 Jan 1986

AB Thalidomide and two analogues, EM87 and EM12, inhibited the attachment of tumor cells to concanavalin A-coated surfaces only if the drugs were first incubated with hepatic microsomes and cofactors. Most agents that inhibit attachment are demonstrated teratogens. Thalidomide undergoes spontaneous hydrolysis to at least 12 products in saline buffered to a pH of greater than 7. These hydrolysis products did not inhibit attachment nor could they be activated to inhibitory products with hepatic microsomes. Similarly EM12 and EM 87 hydrolysis products were neither inhibitory nor substrates for activation. If the three drugs were incubated in buffered saline, there was a progressive decline in their ability to act as substrates for activation to an inhibitory product. It was possible to remove microsomes from the incubation mixture following drug activation by centrifugation. This microsome-free mixture inhibited cell attachment. When mouse ovarian tumor (MOT) cells were added to the microsome-free mixture, attachment was inhibited. However, if the activated drugs were incubated in saline, there was a progressive decline in their ability to inhibit attachment. Decay rates differed for the three compounds. At a pH of 7.4, thalidomide, EM87, and EM12 required 3 h, 1h and 6h, respectively, to decay to control levels. These relative rates of decay are consistent with the relative teratogenicity of the three drugs.

L5 ANSWER 13 OF 63 MEDLINE on STN
ACCESSION NUMBER: 84231518 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6732864
TITLE: Teratogen metabolism: activation of thalidomide and thalidomide analogues to products that inhibit the attachment of cells to concanavalin A coated plastic surfaces.
AUTHOR: Braun A G; Weinreb S L
SOURCE: Biochemical pharmacology, (1984 May 1) Vol. 33, No. 9, pp. 1471-7.
Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 198406
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 22 Jun 1984

AB Thalidomide metabolites inhibited the attachment of tumor cells to concanavalin A coated polyethylene surfaces. Thalidomide, itself, was non-inhibitory. Thalidomide activation to inhibitory products required hepatic microsomes, an NADPH-generating system, and molecular oxygen. Production of inhibitory metabolites was unaffected by either epoxide hydrolase or 1,2-epoxy-3,3,3-trichloropropane (TCPO), an inhibitor of epoxide hydrolase endogenous to hepatic S9 fraction. Therefore, the attachment inhibitor was probably not an arene oxide. Inhibition was not accompanied by cytotoxicity, as judged by trypan blue exclusion. Although uninduced hepatic microsomes from mice, rats and dogs had similar abilities to activate thalidomide, microsomes from Aroclor 1254 induced rats were relatively inactive in the system. Inhibitory metabolites were generated from the thalidomide analogues EM8 , EM12 , EM16 , EM87 , EM136 , EM255 , E350 , phthalimide, phthalimido-phthalimide, indan, 1- indanone and 1,3- indandione . Glutarimide , glutamic acid and phthalic acid did not activate to inhibitory products.

L5 ANSWER 14 OF 63 MEDLINE on STN
ACCESSION NUMBER: 83136405 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7161406
TITLE: The use of vital and morbidity statistics for the detection of adverse drug reactions and for monitoring of drug safety.
AUTHOR: Stolley P D
SOURCE: Journal of clinical pharmacology, (1982 Nov-Dec) Vol. 22, No. 11-12, pp. 499-504.
Journal code: 0366372. ISSN: 0091-2700.
Report No.: PIP-015015; POP-00119443.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population; AIDS
ENTRY MONTH: 198304
ENTRY DATE: Entered STN: 18 Mar 1990
Last Updated on STN: 1 Nov 2002
Entered Medline: 7 Apr 1983

AB Several examples of the use of vital statistics in drug epidemiology are described. The death rates for asthma remained stable from about 1860-1960 in the UK, about 0.5/100,000. In 1961 the rates began to rise, and after 1967 they declined; in the 1970s the rates almost approached pre-epidemic levels. The rates were found to vary with the use of isoproterenol-containing nebulizers. Investigations into the relationship between thromboembolism pulmonary embolism, and myocardial infarction and oral contraceptive (OC) usage showed an increase in death rates beginning after the introduction of OCs in 1960-61 in women at risk. Subacute myelo-optic neuropathy was an unexplained disease until Japanese investigators linked its occurrence to ingestion of the halogenated hydroxyquinoline drugs used to treat nonspecific gastroenteritis; seasonal outbreaks of the disease were linked to seasonal gastroenteritis. Animal experiments conclusively linked the drug to the disease. A Swedish report implicated the antihypertensive drug methyldopa as a possible cause of cancer of the biliary ducts. Links between thalidomide and phocomelia, saccharin or cyclamates and bladder cancer, diethylstilbestrol and vaginal cancer, and estrogens and endometrial cancer are discussed. Drug-monitoring systems, the collection of vital statistics and observations by clinicians all contribute to understanding drug-induced disease. Changes in disease incidence or emergency of new syndromes in areas where certain drugs are heavily used should be compared to areas where they are seldom used.

L5 ANSWER 15 OF 63 MEDLINE on STN
ACCESSION NUMBER: 81184009 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7225125
TITLE: Thalidomide metabolite inhibits tumor cell attachment to concanavalin A coated surfaces.
AUTHOR: Braun A G; Dailey J P
CONTRACT NUMBER: CA-12662-07 (NCI)
SOURCE: Biochemical and biophysical research communications, (1981 Feb 27) Vol. 98, No. 4, pp. 1029-34.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 198106

ENTRY DATE: Entered STN: 16 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 25 Jun 1981

L5 ANSWER 16 OF 63 MEDLINE on STN
ACCESSION NUMBER: 75153202 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1127582
TITLE: Possible antineoplastic agents I.
AUTHOR: De A U; Pal D
SOURCE: Journal of pharmaceutical sciences, (1975 Feb) Vol. 64, No. 2, pp. 262-6.
Journal code: 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197508
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 10 Mar 1990
Entered Medline: 4 Aug 1975

AB A few thalidomide and glutarimide derivatives were synthesized. Several compounds possessed significant antineoplastic activity against Ehrlich ascites carcinoma in Swiss albino mice.,

L5 ANSWER 17 OF 63 MEDLINE on STN
ACCESSION NUMBER: 75070562 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 4140679
TITLE: Human experiences related to adverse drug reactions to the fetus or neonate from some maternally administered drugs.
AUTHOR: Shirkey H C
SOURCE: Advances in experimental medicine and biology, (1972) Vol. 27, pp. 17-30.
Journal code: 0121103. ISSN: 0065-2598.
Report No.: PIP-723949; POP-00015296.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 197503
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 1 Nov 2002
Entered Medline: 17 Mar 1975

AB This is a review of known periods in utero during which drugs alter the process of growth; effects may be shown on the fetus or the newborn and vary with the stage of development of the fetus when exposed. Other variables are the mother and the placenta. There is no safe animal screening mechanism, the human test is by ordeal, and more clinical monitoring and reporting are needed. Cancer chemotherapeutic agents exert their maximal effects on rapidly dividing cells and are therefore hazardous during pregnancy; the greatest risk is in the 1st trimester. In the thalidomide experience the critical days were the 22nd and 23rd days after conception. Masculinizing drugs such as testosterone and other androgenic steroids have been implicated as affecting the female fetus when given early in pregnancy. Oral contraceptives taken by an already pregnant woman are a hazard because of these progestational agents. Progesterone alone is unlikely to cause masculinization but other progestins may cause such changes. Carcinogenesis may develop later in females born of mothers who are treated with diethylstilbestrol to prevent miscarriage. Many antithyroid drugs have caused neonatal goiter. Maternal ingestion of iodides during pregnancy (preparations for treating asthma, cough syrups, radio-

contrast media used in diagnoses) is the most frequent cause. Goiter is relatively common in infants whose mothers were treated with propylthiouracil and other antithyroid drugs, yet they usually show normal thyroid function. However, hypothyroidism with cretinism can occur. Lithium, used in psychiatry and as a salt substitute, may alter iodine metabolism and thyroid gland function. It also passes into the milk to continue the potential toxicity. Teratogenic effects in experimental animals suggest other possible effects on infants from lithium and similar drugs.

L5 ANSWER 18 OF 63 MEDLINE on STN
ACCESSION NUMBER: 68088971 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 4229090
TITLE: Effect of transplanted tumor and various agents on liver regeneration during pregnancy.
AUTHOR: Gershbein L L
SOURCE: Rivista di patologia nervosa e mentale, (1966 Aug) Vol. 87, No. 4, pp. 88-92.
Journal code: 0431335. ISSN: 0035-6433.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196802
ENTRY DATE: Entered STN: 1 Jan 1990
Last Updated on STN: 1 Jan 1990
Entered Medline: 13 Feb 1968

L5 ANSWER 19 OF 63 MEDLINE on STN
ACCESSION NUMBER: 68044021 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 4168246
TITLE: [Thalidomide and cancer].
Thalidomid und Tumor.
AUTHOR: Muckter H; More E
SOURCE: Arzneimittel-Forschung, (1966 Feb) Vol. 16, No. 2, pp. 129-34.
Journal code: 0372660. ISSN: 0004-4172.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196801
ENTRY DATE: Entered STN: 1 Jan 1990
Last Updated on STN: 1 Jan 1990
Entered Medline: 12 Jan 1968

L5 ANSWER 20 OF 63 MEDLINE on STN
ACCESSION NUMBER: 67045840 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 5924955
TITLE: Effect of various agents on liver regeneration and Walker tumor growth in partially hepatectomized rats.
AUTHOR: Gershbein L L
SOURCE: Cancer research, (1966 Sep) Vol. 26, No. 9, pp. 1905-8.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196702
ENTRY DATE: Entered STN: 1 Jan 1990

Last Updated on STN: 1 Jan 1990
Entered Medline: 5 Feb 1967

L5 ANSWER 21 OF 63 MEDLINE on STN
ACCESSION NUMBER: 66136696 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 5883469
TITLE: Thalidomide and tumor.
AUTHOR: Muckter H
SOURCE: Antimicrobial agents and chemotherapy, (1965) Vol. 5, pp. 531-8.
Journal code: 0116415. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196608
ENTRY DATE: Entered STN: 1 Jan 1990
Last Updated on STN: 3 Mar 2000
Entered Medline: 13 Aug 1966

L5 ANSWER 22 OF 63 MEDLINE on STN
ACCESSION NUMBER: 65100633 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14296026
TITLE: CLINICAL EXPERIENCES WITH THALIDOMIDE IN PATIENTS WITH CANCER.
AUTHOR: GRABSTALD H; GOLBEY R
SOURCE: Clinical pharmacology and therapeutics, (1965 May-Jun) Vol. 6, pp. 298-302.
Journal code: 0372741. ISSN: 0009-9236.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Dec 1996

L5 ANSWER 23 OF 63 MEDLINE on STN
ACCESSION NUMBER: 65100632 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14296025
TITLE: THALIDOMIDE (N-PHTHALOYLGLUTAMIMIDE) IN THE TREATMENT OF ADVANCED CANCER.
AUTHOR: OLSON K B; HALL T C; HORTON J; KHUNG C L; HOSLEY H F
SOURCE: Clinical pharmacology and therapeutics, (1965 May-Jun) Vol. 6, pp. 292-7.
Journal code: 0372741. ISSN: 0009-9236.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Dec 1996

L5 ANSWER 24 OF 63 MEDLINE on STN
ACCESSION NUMBER: 64152365 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14194333

TITLE: [STUDIES OF THE ANTITUMORAL ACTIVITY OF THALIDOMIDE].
STUDI SULL'ATTIVIT'A ANTITUMORALE DELLA TALIDOMIDE.
AUTHOR: GAETANI M
SOURCE: Giornale italiano di chemioterapia, (1964 Apr-Jun) Vol. 11, pp. 83-6.
Journal code: 17140055R. ISSN: 0017-0445.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Dec 1996

L5 ANSWER 25 OF 63 MEDLINE on STN
ACCESSION NUMBER: 64127325 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14169347
TITLE: THALIDOMIDE: EFFECTS ON EHRLICH ASCITES TUMOR CELLS IN VITRO.
AUTHOR: DIPAOLO J A; WENNER C E
SOURCE: Science (New York, N.Y.), (1964 Jun 26) Vol. 144, pp. 1583.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Dec 1996

L5 ANSWER 26 OF 63 MEDLINE on STN
ACCESSION NUMBER: 64081361 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14123612
TITLE: [TREATMENT OF EXPERIMENTAL TUMORS WITH THALIDOMIDE].
TRATTAMENTO DI TUMORI SPERIMENTALI CON TALIDOMIDE.
AUTHOR: PAGNINI G; DICARLO R
SOURCE: Bollettino della Societa italiana di biologia sperimentale, (1963 Nov 30) Vol. 39, pp. 1360-3.
Journal code: 7506962. ISSN: 0037-8771.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Dec 1996

L5 ANSWER 27 OF 63 MEDLINE on STN
ACCESSION NUMBER: 64058880 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14101198
TITLE: IN VITRO TEST SYSTEMS FOR CANCER CHEMOTHERAPY.
II. CORRELATION OF IN VITRO INHIBITION OF DEHYDROGENASE AND GROWTH WITH IN VIVO INHIBITION OF EHRLICH ASCITES TUMOR.
AUTHOR: DIPAOLO J A
SOURCE: Proceedings of the Society for Experimental Biology and Medicine. Society for Experimental Biology and Medicine

(New York, N.Y.), (1963 Nov) Vol. 114, pp. 384-7.
Journal code: 7505892. ISSN: 0037-9727.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Dec 1996

L5 ANSWER 28 OF 63 MEDLINE on STN
ACCESSION NUMBER: 64039115 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14081473
TITLE: [CLINICAL IMPROVEMENTS OBTAINED IN ADVANCED CANCER PATIENTS WITH TREATMENT WITH THALIDOMIDE ASSOCIATED WITH HORMONES] .. MELHORAS CL'INICAS OBTIDAS EM DOENTES CANCEROSOS AVAN CADOS COM TRATAMENTO PELA TALIDOMIDA ASSOCIADA A HORM ONIOS.
AUTHOR: MAUAD M J
SOURCE: Anais paulistas de medicina e cirurgia, (1963 Jul) Vol. 86, pp. 13-40.
Journal code: 0373070. ISSN: 0003-245X.
PUB. COUNTRY: Brazil
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Portuguese
FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Dec 1996

L5 ANSWER 29 OF 63 MEDLINE on STN
ACCESSION NUMBER: 62221950 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14029957
TITLE: Absence of carcinostatic effect of thalidomide with respect to 2 grafted tumors.
AUTHOR: JURET P; AUBERT C
SOURCE: Comptes rendus des seances de la Societe de biologie et de ses filiales, (1963 Jun 10) Vol. 157, pp. 246-9.
Journal code: 7505439. ISSN: 0037-9026.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Nov 1998

L5 ANSWER 30 OF 63 MEDLINE on STN
ACCESSION NUMBER: 62149843 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 13958105
TITLE: Absence of carcinostatic effect of thalidomide with respect to 2 grafted tumors.
AUTHOR: JURET P; AUBERT C
SOURCE: Comptes rendus des seances de la Societe de biologie et de ses filiales, (1963 Jun 10) Vol. 157, pp. 246-9.
Journal code: 7505439. ISSN: 0037-9026.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French

FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Nov 1998

L5 ANSWER 31 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:214219 CAPLUS Full-text
DOCUMENT NUMBER: 120:214219
TITLE: Inhibition of tumor necrosis factor-alpha by thalidomide in magnesium deficiency
AUTHOR(S): Weglicki, William B.; Stafford, Richard E.; Dickens, Benjamin F.; Mak, I. Tong; Cassidy, Marie M.; Phillips, Terry M.
CORPORATE SOURCE: Med. Cent., George Washington Univ., Washington, DC, 20037, USA
SOURCE: Molecular and Cellular Biochemistry (1993), 129(2), 195-200
CODEN: MCBIB8; ISSN: 0300-8177
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of thalidomide on circulating cytokines and myocardial lesion formation was investigated in Mg-deficient rats. After two weeks on a Mg-deficient diet, rats show an increase in circulating levels of tumor necrosis factor-alpha and interleukin 1. Thalidomide (1 mg/day) caused a complete inhibition of the increase in circulating tumor necrosis factor-alpha levels, without having an effect in interleukin 1. However, a marked increased in cardiomyopathic lesion formation was observed in Mg-deficient animals treated with thalidomide; possible mechanisms for thalidomide's enhancement of myocardial injury are discussed.

L5 ANSWER 32 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:508464 CAPLUS Full-text
DOCUMENT NUMBER: 119:108464
TITLE: Thalidomide inhibits the replication of human immunodeficiency virus type 1
AUTHOR(S): Makonkawkeyoon, Sanit; Limson-Pobre, Rhona N. R.; Moreira, Andre L.; Schauf, Victoria; Kaplan, Gilla
CORPORATE SOURCE: Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1993), 90(13), 5974-8
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thalidomide, a selective inhibitor of tumor necrosis factor α (TNF-α) synthesis, suppresses the activation of latent human immunodeficiency virus type 1 (HIV-1) in a monocytoid (U1) line. The inhibition is dose dependent and occurs after exposure of the cells to recombinant TNF-α, phorbol myristate acetate, lipopolysaccharide, and other cytokine combinations. Associated with HIV-1 inhibition is a reduction in agonist-induced TNF-α protein and mRNA production Thalidomide inhibition of virus replication in the phorbol myristate acetate- and recombinant TNF-α-stimulated T-cell line ACH-2 is not observed The presence of thalidomide also inhibits the activation of virus in the peripheral blood mononuclear cells of 16 out of 17 patients with advanced HIV-1 infection and AIDS. These results suggest the use of thalidomide in a clin. setting to inhibit both virus replication and the TNF-α-induced systemic toxicity of HIV-1 and opportunistic infections.

L5 ANSWER 33 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:204908 CAPLUS Full-text
DOCUMENT NUMBER: 118:204908
TITLE: Thalidomide exerts its inhibitory action on tumor necrosis factor α by enhancing mRNA degradation
AUTHOR(S): Moreira, Andre L.; Sampaio, Elizabeth P.; Zmuidzinas, Antonina; Frindt, Paula; Smith, Kendall A.; Kaplan, Gilla
CORPORATE SOURCE: Dep. Cell. Physiol. Immunol., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Journal of Experimental Medicine (1993), 177(6), 1675-80
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mechanism of thalidomide inhibition of lipopolysaccharide (LPS)-induced tumor necrosis factor α (TNF-α) production was examined; the drug enhanced the degradation of TNF-α mRNA. The half-life of the mol. was reduced from .apprx.30 to .apprx.17 min in the presence of 50 μg/mL of thalidomide. Inhibition of TNF-α production was selective, as other LPS-induced monocyte cytokines were unaffected. Pentoxifylline and dexamethasone, two other inhibitors of TNF-α production, are known to exert their effects by means of different mechanisms, suggesting that the three agents inhibit TNF-α synthesis at distinct points of the cytokine biosynthetic pathway. These observations provide an explanation for the synergistic effects of these drugs. The selective inhibition of TNF-α production makes thalidomide an ideal candidate for the treatment of inflammatory conditions where TNF-α-induced toxicities are observed and where immunity must remain intact.

L5 ANSWER 34 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:212678 CAPLUS Full-text
DOCUMENT NUMBER: 116:212678
TITLE: Prolonged treatment with recombinant interferon γ induces erythema nodosum leprosum in lepromatous leprosy patients
AUTHOR(S): Sampaio, Elizabeth P.; Moreira, Andre L.; Sarno, Euzenir N.; Malta, Ana M.; Kaplan, Gilla
CORPORATE SOURCE: Lab. Cell. Physiol. Immunol., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Journal of Experimental Medicine (1992), 175(6), 1729-37
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Patients with borderline and lepromatous leprosy were selected for a prolonged trial with recombinant interferon γ (rIFN-γ). Patients received 30 μg intradermally for 6 injections over a 9-day period, and then either 100 μg intradermally every 1 mo for 10 mo or every 2 wk for 5 mo (total, 1.2 mg). Erythema nodosum leprosum (ENL) was induced in 60% of the patients within 6-7 mo, as compared with an incidence of 15% per yr with multiple drug therapy alone. The mean whole-body reduction in bacterial index over the first 6 mo was 0.9 log units. Cutaneous induration at the intradermal injection sites of ≥15 mm predicted the development of a subsequent reactional state. Monocytes obtained from patients receiving the lymphokine demonstrated an increased respiratory burst and a 2.5-5.1-fold increase in tumor necrosis factor α (TNF-

α) secretion in response to agonists. Patients in ENL had an even higher release of TNF-α from monocytes as well as high levels of TNF-α in the plasma (2000 pg/mL). Thalidomide therapy was required to treat the systemic manifestations of ENL. Control of toxic symptoms with thalidomide was associated with a 50-80% reduction in agonist-stimulated monocyte TNF-α secretion. IFN-γ enhanced the monocyte release of TNF-α by 3-7.5-fold (agonist dependent) when added to patient's cells in vitro, and this could be suppressed by the in vitro addition of 10 μg/mL of thalidomide.

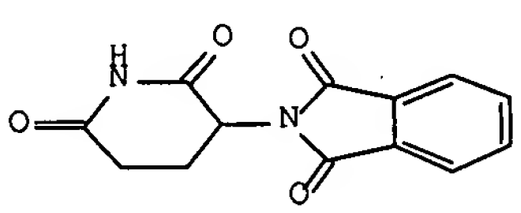
L5 ANSWER 35 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:156793 CAPLUS Full-text
DOCUMENT NUMBER: 114:156793
TITLE: Thalidomide selectively inhibits tumor necrosis factor α production by stimulated human monocytes
AUTHOR(S): Sampaio, Elizabeth P.; Sarno, Euzenir N.; Galilly, Ruth; Cohn, Zanvil A.; Kaplan, Gilla
CORPORATE SOURCE: Lab. Cell. Physiol. Immunol., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Journal of Experimental Medicine (1991), 173(3), 699-703
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thalidomide selectively inhibits the production of human monocyte tumor necrosis factor-α (TNF-α) when these cells are triggered with lipopolysaccharide and other agonists in culture. A 40% inhibition occurs at the clin. achievable concentration of 1 μg/mL. The amount of total protein and individual proteins labeled with [35S]methionine detected by SDS-PAGE are not affected by thalidomide. The amts. of interleukin 1β (IL-1β), IL-6, and granulocyte/macrophage colony-stimulating factor produced by monocytes remain unaltered. The selectivity of this drug may be useful in determining the role of TNF-α in vivo and modulating its toxic effects in a clin. setting.

L5 ANSWER 36 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:52389 CAPLUS Full-text
DOCUMENT NUMBER: 110:52389
TITLE: Evaluation of two in vitro assays to screen for potential developmental toxicants
AUTHOR(S): Steele, Vernon E.; Morrissey, Richard E.; Elmore, Eugene L.; Gurganus-Rocha, Deborah; Wilkinson, Betty P.; Curren, Rodger D.; Schmetter, Barry S.; Louie, Audrey T.; Lamb, James C., IV; Yang, Li L.
CORPORATE SOURCE: Northrop Services, Inc., Research Triangle Park, NC, 27709, USA
SOURCE: Fundamental and Applied Toxicology (1988), 11(4), 673-84
CODEN: FAATDF; ISSN: 0272-0590
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To evaluate two in vitro assays for their ability to detect known developmental toxicants and nontoxicants, a series of 44 coded compds. were assayed by 2 independent labs. using standardized protocols. The 2 test systems were the human embryonic palatal mesenchymal cell growth inhibition assay and the mouse ovarian tumor cell attachment inhibition assay. After all compds. were tested, they were decoded and ranked according to the min. IC50

value (the millimolar concentration of compound which inhibits growth or attachment by 50% compared to the solvent control) from either test. The in vitro test result concordance with established in vivo animal and human test results was examined over a wide range of concentration levels (above which the in vitro results were called pos. and below which they were considered neg.). A pos. response from either test was defined as a pos. in vitro response. Concordance was defined as the number of correct responses divided by the number of chems. tested. At the 1-mM level, the concordance of data from the combined in vitro assays with the in vivo data was 66% in one laboratory and 58% in the other. The maximum agreement between the combined in vitro and in vivo data was reached at the 20-mM level, where there was a 73 and 74% concordance of results in the 2 labs. At that level, there was a 16 and 10% incidence of false neg. results, and a 54 and 77% incidence of false pos. results. A portion of these false neg. compds. may require metabolic activation. The use of either assay alone was not as accurate as using a pos. result from either test. Agreement of the in vitro data at the 10-mM level with available human data was 71 and 75% for each laboratory Thus, 2 assays are complimentary and the combination of these assays could be useful as a preliminary screen to establish priorities for in vivo developmental toxicity testing.

L5 ANSWER 37 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN

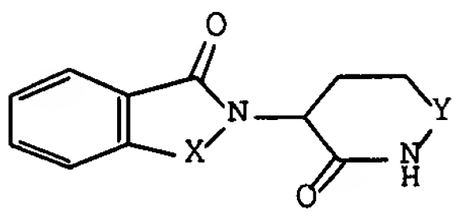
ACCESSION NUMBER: 1986:124742 CAPLUS Full-text
DOCUMENT NUMBER: 104:124742
TITLE: Teratogen metabolism: thalidomide activation is mediated by cytochrome P 450
AUTHOR(S): Braun, Andrew G.; Harding, Fiona A.; Weinreb, Steven L.
CORPORATE SOURCE: Dep. Appl. Biol. Sci., Massachusetts Inst. Technol., Cambridge, MA, 01239, USA
SOURCE: Toxicology and Applied Pharmacology (1986), 82(1), 175-9
CODEN: TXAPA9; ISSN: 0041-008X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Metabolite of thalidomide (I) [50-35-1] generated by hepatic microsomes inhibited the attachment of tumor cells to concanavalin A-coated polyethylene. Evidence that metabolite formation is mediated by microsomal cytochrome P 450 [9035-51-2] is presented. Microsomes incubated with I underwent a type I spectral shift. Metabolite formation was reduced or eliminated by CO, SKF-525A [62-68-0], metyrapone [54-36-4], and N-octylamine [111-86-4]. Superoxide dismutase [9054-89-1] treatment had no effect. Metabolite formation required microsomes and NADPH and was dependent on the length of 37° incubation. The metabolite could be isolated by successive hexane and CHCl3 extns. It is likely, the inhibitory I metabolite was generated by a minor cytochrome P 450 species. Whether this I metabolite is involved in the drug's teratogenic activity remains to be shown.

L5 ANSWER 38 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:555559 CAPLUS Full-text
DOCUMENT NUMBER: 103:155559
TITLE: Teratogen metabolism: spontaneous decay products of thalidomide and thalidomide analogs are not bioactivated by liver microsomes
AUTHOR(S): Braun, Andrew G.; Weinreb, Steven L.
CORPORATE SOURCE: Dep. Appl. Biol. Sci., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Teratogenesis, Carcinogenesis, and Mutagenesis (1985), 5(3), 149-58
CODEN: TCMUD8; ISSN: 0270-3211
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



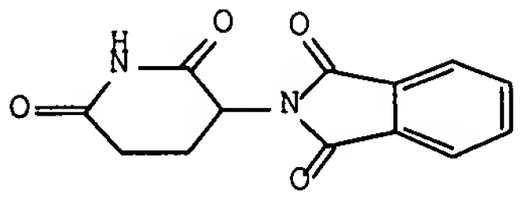
I, X=Y=CO
II, X=SO_2, Y=CH_2
III, X=CH_2, Y=CO

AB Thalidomide (I) [50-35-1] and 2 analogs, EM 87 (II) [49785-74-2], and EM 12 (III) [26581-81-7], inhibited the attachment of tumor cells to concanavalin A-coated surfaces if the drugs were 1st incubated with hepatic microsomes and cofactors. Most agents that inhibit attachment are demonstrated teratogens. I underwent spontaneous hydrolysis to at least 12 products in saline buffered to a pH >7. These hydrolysis products did not inhibit attachment nor could they be activated to inhibitory products with hepatic microsomes. Similarly, II and III hydrolysis products were neither inhibitory nor substrates for activation. If the 3 drugs were incubated in buffered saline, there was a progressive decline in their ability to act as substrates for activation to an inhibitory product. It was possible to remove microsomes from the incubation mixture following drug activation by centrifugation. This microsome-free mixture inhibited cell attachment. When mouse ovarian tumor (MOT) cells were added to the microsome-free mixture, attachment was inhibited. However, if the activated drugs were incubated in saline, there was a progressive decline in their ability to inhibit attachment. Decay rates differed for the 3 compds. At a pH of 7.4, I, II, and III required 3, 1, and 6 h, resp., to decay to control levels. These relative rates of decay are consistent with the relative teratogenicity of the 3 drugs.

L5 ANSWER 39 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:543568 CAPLUS Full-text
DOCUMENT NUMBER: 101:143568
TITLE: Teratogen metabolism: spontaneous decay hydrolysis products of thalidomide and thalidomide analog are not activated by liver microsomes
AUTHOR(S): Braun, A. G.; Weinreb, S. L.
CORPORATE SOURCE: Dep. Radiat. Ther., Harvard Med. Sch., Boston, MA, USA
SOURCE: Report (1983), DOE/ER/60070-T3; Order No. DE84006117, 18 pp. Avail.: NTIS

From: Energy Res. Abstr. 1984, 9(9), Abstr. No. 17444

DOCUMENT TYPE: Report
LANGUAGE: English
GI

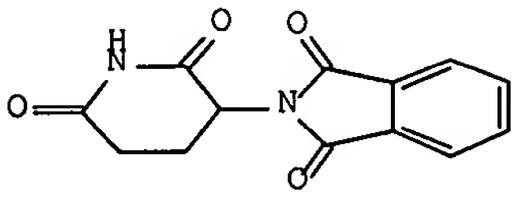


I

AB Thalidomide (I) [50-35-1] and 2 analogs, EM 87 [49785-74-2] and EM 12 [26581-81-7], inhibit the attachment of tumor cells to concanavalin A-coated surfaces only if the drugs are treated with hepatic microsomes and cofactors. Preincubation of these drugs in buffered saline at 37° results in a progressive decline in their ability to be activated to inhibitory products. Similarly, postincubation of the inhibitory products leads to a decline in their ability to inhibit attachment. Decay rates differ for the 3 compds. I, EM 87, and EM 12 require 3, 1, and 6 h, resp., to decline to control levels. These relative rates of decay are consistent with the relative teratogenicity of the 3 drugs.

L5 ANSWER 40 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:503515 CAPLUS Full-text
DOCUMENT NUMBER: 101:103515
TITLE: Teratogen metabolism: activation of thalidomide and thalidomide analogs to products that inhibit the attachment of cells to concanavalin A coated plastic surfaces
AUTHOR(S): Braun, Andrew G.; Weinreb, Steven L.
CORPORATE SOURCE: Dep. Radiat. Ther., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Biochemical Pharmacology (1984), 33(9), 1471-7
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thalidomide (I) [50-35-1] metabolites inhibited the attachment of tumor cells to concanavalin A [11028-71-0]-coated polyethylene surfaces. I, itself, was noninhibitory. I activation to inhibitory products required hepatic microsomes, an NADPH-generating system, and O. Production of inhibitory metabolites was unaffected by either epoxide hydrolase or 1,2-epoxy-3,3,3-trichloropropane, an inhibitor of epoxide hydrolase endogenous to hepatic S9 fraction. Therefore, the attachment inhibitor was probably not an arene oxide. Inhibition was not accompanied by cytotoxicity, as judged by trypan blue exclusion. Although uninduced hepatic microsomes from mice, rats, and dogs had similar abilities to activate I, microsomes from Aroclor 1254-induced rats were relatively inactive in the system. Inhibitory metabolites were generated from the I analogs EM8 [16477-31-9], EM12 [26581-81-7], EM16 [26581-91-9], EM87 [49785-74-2], EM136 [42472-96-8], EM255 [79458-80-3], E350 [303-31-1], phthalimide [85-41-6], phthalimidophthalimide [4388-29-8], indan [496-11-7], 1-indanone [83-33-0] and 1,3-indandione [606-23-5]. Glutarimide [1121-89-7], glutamic acid [56-86-0], and phthalic acid [88-99-3] did not activate to inhibitory products.

L5 ANSWER 41 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:483948 CAPLUS Full-text
DOCUMENT NUMBER: 101:83948
TITLE: Teratogen metabolism: activation of thalidomide and thalidomide analogs to products that inhibit the attachment of cells to concanavalin A coated plastic surfaces. Revised version
AUTHOR(S): Weinreb, S. L.
CORPORATE SOURCE: Dep. Radiat. Ther., Harvard Med. Sch., Boston, MA, USA
SOURCE: Report (1982), DOE/ER/60070-T1; Order NO. DE84006118, 32 pp. Avail.: NTIS
From: Energy Res. Abstr. 1984, 9(8), Abstr. No. 15071
DOCUMENT TYPE: Report
LANGUAGE: English
GI



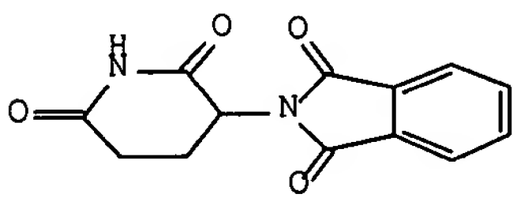
I

AB Thalidomide (I) [50-35-1] metabolites inhibit the attachment of tumor cells to concanavalin A-coated polyethylene surfaces. I itself is noninhibitory. I activation to inhibitory products requires hepatic microsomes, an NADPH generating system and mol. O. Production of inhibitory metabolites is unaffected by either epoxide hydrolase or TCPO, an inhibitor of epoxide hydrolase endogenous to hepatic S9 fraction. Therefore, the attachment inhibitor is probably not an arene oxide. Inhibition is not accompanied by cytotoxicity as judged by trypan blue exclusion. Although uninduced hepatic microsomes from mice, rats, and dogs have similar ability to activate I microsomes from Aroclor 1254 induced rats are relatively inactive in the system. Inhibitory metabolites can be generated from the I analogs EM8 [16477-31-9], EM12 [26581-81-7], EM16 [26581-91-9], EM87 [49785-74-2], EM136 [42472-96-8], EM255 [79458-80-3], E350 [303-31-1], phthalimide [85-41-6] phthalimido-phthalimide [4388-29-8] indan [496-11-7], 1-indanone [83-33-0], and 1,3-indandione [606-23-5]. Glutarimide [1121-89-7], glutamic acid [56-86-0] and phthalic acid [88-99-3] do not activate to inhibitory products.

L5 ANSWER 42 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:175852 CAPLUS Full-text
DOCUMENT NUMBER: 96:175852
TITLE: Quantitative correspondence between the in vivo and in vitro activity of teratogenic agents
AUTHOR(S): Braun, Andrew G.; Buckner, Christine A.; Emerson, David J.; Nichinson, Bradley B.
CORPORATE SOURCE: Dep. Radiat. Ther., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1982), 79(6), 2056-60
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Seventy-four teratogenic and 28 nonteratogenic agents were tested in a developed in vitro teratogen assay. The assay identified teratogens by their

ability to inhibit attachment of ascites tumor cells to plastic surfaces coated with concanavalin A. There was a qual. agreement between in vivo animal data and in vitro activity for 81 of 102 agents (79%). Quant. anal. showed a highly significant correlation coefficient of 0.69 between the inhibitory in vitro dose and the lowest reported teratogenic dose for 54 of 60 inhibitory teratogens. The doses analyzed ranged over 5 orders of magnitude. These results were interpreted to mean that attachment inhibition in concert with other, complementary, in vitro assay systems can become a useful method for the assessment of the teratogenic potential of environmental agents.

L5 ANSWER 43 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:132131 CAPLUS Full-text
DOCUMENT NUMBER: 94:132131
TITLE: Thalidomide metabolite inhibits tumor cell attachment to concanavalin A-coated surfaces
AUTHOR(S): Braun, Andrew G.; Dailey, James P.
CORPORATE SOURCE: Dep. Radiat. Therapy, Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Biochemical and Biophysical Research Communications (1981), 98(4), 1029-34
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

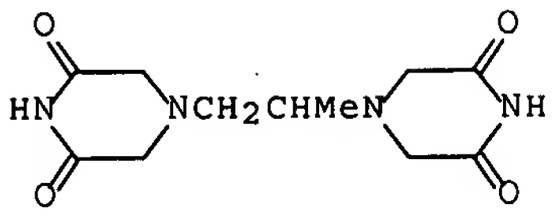


I

AB The inhibitory effect of drug treatment on tumor cell attachment to plastic surfaces coated with concanavalin A [11028-71-0] correlated well with the in vivo teratogenicity of the drug. The effects of thalidomide (I) [50-35-1] and some of its metabolites were examined for inhibitory activity. While I and its hydrolysis products did not alter attachment, metabolites of I produced by incubation of the drug with murine liver microsomes were inhibitory. Generation of inhibitory products required the presence of glucose-6-phosphate, NADP, glucose-6-phosphate dehydrogenase, and MgCl2. The degree of inhibition was dependent on the duration of incubation at 37°. These results suggest a model for the teratogenic action of I in which metabolites of the drug alter cell surface function leading to interference with normal morphogenic cell to cell interactions.

L5 ANSWER 44 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:537359 CAPLUS Full-text
DOCUMENT NUMBER: 85:137359
TITLE: Factors related to tumor spread in the body
AUTHOR(S): Boggust, W. A.
CORPORATE SOURCE: Dep. Exp. Med., Trinity Coll., Dublin, Ire.
SOURCE: Advances in Tumour Prevention, Detection and Characterization (1976), 3(Biol. Charact. Hum. Tumours, Proc. Int. Symp., 6th, 1975), 383-90
CODEN: APDCDT

DOCUMENT TYPE: Journal
LANGUAGE: English
GI



II

AB In exts. of human cancers, cathepsins B, C, and D, leucine aminopeptidase [9001-61-0], glucosaminidase [9027-56-9], acid and neutral collagenase [9001-12-1], and fibrinolysin [9001-90-5] activities were found. Collagenase was blocked by the chelating agents dimercaptopropanol (BAL) [59-52-9], EDTA [60-00-4], and o-phenanthroline (I) [66-71-7], and the cytostatic drug ICRF-159 (II) [21416-87-5]. Combinations of I and II were synergistic. II also inhibited cathepsins C and B1 and probably glucosaminidase, but not cathepsin D or leucineaminopeptidase. Mice bearing implanted carcinoma excised on the 10th day, died from lung metastases within 34 days unless otherwise treated. Survival periods were increased by II, but not by I alone. Combinations of I and II substantially increased the survival period. Thus, I and II by acting as enzyme inhibitors and cytotoxic agents they helped to inhibit primary tumor growth and prevent metastases.

L5 ANSWER 45 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:123495 CAPLUS Full-text
DOCUMENT NUMBER: 74:123495
TITLE: Immunosuppressant action of thalidomide and prednisolone in rats with experimentally-induced neoplasia
AUTHOR(S): Guidetti, Ettore; Moiraghi-Ruggenini, A.; Errigo, E.; Martelli, M. P.
CORPORATE SOURCE: Ist. Ig., Univ. Torino, Turin, Italy
SOURCE: Cancro (1969), 22(5), 503-12
CODEN: CAROAF; ISSN: 0008-5480
DOCUMENT TYPE: Journal
LANGUAGE: Italian
GI For diagram(s), see printed CA Issue.
AB A particular test of complement activity elicited by reaction of serum factor with an RNA isolated from a mutant of S. cerevisiae was performed in order to analyze the activity of thalidomide (I) and prednisolone (II) as immunosuppressant drugs in rats. I or II were given i.p. to rats with a mean weight of 140 g for 10 consecutive days at the resp. daily doses of 100 mg (as Na salt) and 10 mg. Half of the rats were previously inoculated e.g. with 6 + 106 cells of Yoshida tumor. In all the control animals without tumor the production of the serum factor was not inhibited whereas increasing nos. of rats inoculated with tumor cells showed a deficiency of the factor (20% of the rats at the 1st day, 90% at the 5th, 100% at the 9th and 10th day). I and II were without effect in control rats whereas in rats inoculated with tumor cells an addnl. immunosuppressant action was evidenced (100% of the rats showed deficiency of the serum factor at the 5th day with I and at the 7th day with II). In .apprx.10% of the above rats the reaction for the serum factor turned pos. at the 7th-10th day with I but not with II.

L5 ANSWER 46 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1970:98435 CAPLUS Full-text
DOCUMENT NUMBER: 72:98435
TITLE: Potentiating effect of thalidomide on methylcholanthrene oncogenesis in mice
AUTHOR(S): Miura, Mitsuhiko; Southam, Chester M.; Wuest, Heinz M.
CORPORATE SOURCE: Sloan Kettering Inst. for Cancer Res., New York, NY, USA
SOURCE: Experientia (1970), 26(3), 305-6
CODEN: EXPEAM; ISSN: 0014-4754
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The i.p. administration of thalidomide (25 mg/day for 5 days in each of 4 consecutive weeks) to mice increased the number of papillomas which developed in response to applications of methylcholanthrene (I) (0.2 ml of a 1% solution for 5 consecutive days) to skin; thalidomide was started 1 week before I and was continued until 1 or 2 weeks after the application of I had stopped. There was no evidence that thalidomide enhanced I oncogenesis via immunosuppression. The oral administration of thalidomide at the same dosage and on the same schedule did not significantly increase the oncogenic response to I.

L5 ANSWER 47 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:502238 CAPLUS Full-text
DOCUMENT NUMBER: 65:102238
ORIGINAL REFERENCE NO.: 65:19127g-h
TITLE: N-Phthaloylglutamimide (thalidomide) in the symptomatic treatment of vomiting
AUTHOR(S): Traldi, A.; Vaccari, G. L.; Davoli, G.
CORPORATE SOURCE: Ist. Patol. Med., Univ., Modena, Italy
SOURCE: Cancro (1965), 18(4), 336-41
CODEN: CAROAF; ISSN: 0008-5480
DOCUMENT TYPE: Journal
LANGUAGE: Italian

AB The effectiveness of thalidomide(I) was studied in 14 cancer patients (group 1) with persistent vomiting and in 21 subjects with hemolymphopathy (group 2) in whom vomiting occurred upon intravenous administration of mechlorethamineHCl (II). I was given in a dose of 60 mg. every 8 hrs. to the cancer patients and 60 mg. 0.5 hr. before, and 1 and 4 hrs. after, injection of II to the 2nd group. Antiemetic action was immediate and effective in 9 subjects of the 1st group, and of moderate effectiveness in 3 subjects. In the 2nd group, all 21 patients responded pos., the results being comparable to those obtained with known antiemetics, e.g., phenothiazine and its derivs. I might block afferent impulses of visceral origin, or might interrupt the reflex arc of vomiting in the bulbar centers.

L5 ANSWER 48 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:501712 CAPLUS Full-text
DOCUMENT NUMBER: 65:101712
ORIGINAL REFERENCE NO.: 65:19035g-h,19036a-b
TITLE: Stimulation of growth by subliminal concentrations of growth-inhibiting substances
AUTHOR(S): Rauen, H. M.; Norpoth, K.
CORPORATE SOURCE: Univ. Muenster, Germany
SOURCE: Arzneimittel-Forschung (1966), 16(8), 1001-7
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal

LANGUAGE: German

AB 2-Amino-4,6-dimethylpyrimidine at 50-200 γ/ml. stimulated growth of Neurospora crassa, but at higher concns., it was inhibitory. 4,5-Diamino-1,3-dimethyl-2,6-dihydroxypyrimidine at 10-50 γ/ml. stimulated N. crassa growth, but at 200-2000 γ/ml. inhibited it. 2-Amino-4-chloropyrimidine and 2-amino4-chloro-6-methylpyrimidine produced similar results. Actinomycin D (1-3 γ/ml.) stimulated growth of Sordaria macrospora, but at 5 γ/ml. inhibited growth. Thalidomide (≤200 γ/ml.). stimulated growth of Lactobacillus fermenti, 500-1000 γ/ml. inhibited growth. N,N-Bis(2-chloroethyl)-N',O- propylenephosphoric acid ester diamide and bis-(β-chloroethyl)amine- HCl at low concns. stimulated growth of yeasts, lactobacilli, and Escherichia coli, but inhibited growth at high concns. The coplanar heterooligobases, HR-1887, HR-2257, and HR-2074, shifted the growth curve of Streptomyces faecalis R to the right. Sandoz SP-G (which contains podophyllotoxin β-D-benzylidene glucoside, 4'-demethylpodophyllotoxin β-D-benzylidene glucoside, and some other natural compds.), derived from rhizomes of Podophyllure emodi, did not inhibit 2 strains of Micrococcus pyrogenes, E. coli, Proteus vulgaris, Saccharomyces cerevisiae, or Amoeba proteus; it slightly inhibited L. casei, L. arabinosus, L. mesenteroides, and Bacillus cereus; but it greatly inhibited growth of L. fermenti and stimulated growth of S. faecalis. Sandoz SP-I (podophyllic acid ethyl hydrazide) had a much weaker effect on L. fermenti, but a similar effect on L. casei and B. cereus compared with Sandoz SP-G. Sandoz SP-I did not influence growth of S. faecalis, L. arabinosus or L. mesenteroides. Growth of Jensen sarcoma transplanted on the chorioallantois of hatched hen eggs was stimulated by 20 γ of HR-2074/egg and was inhibited by 500 γ to 1 mg./egg. Sandoz SP-G (100 γ/egg) stimulated the growth of transplanted Voshida sarcoma, whereas 1 mg./egg inhibited growth. Sandoz SP-I produced similar results with Jensens sarcoma and Walker carcinosarcoma. Verrucarin A isolated from Myrothecium verrucaria and anguidin at 1 mg./egg inhibited growth of Yoshida sarcoma but stimulated growth of DS-carcinosarcoma. Low doses of cytostatics can stimulate microbial and tumor growth. 29 references.

L5 ANSWER 49 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:493663 CAPLUS Full-text
DOCUMENT NUMBER: 65:93663
ORIGINAL REFERENCE NO.: 65:17554c-e
TITLE: Effect of various agents on liver regeneration and Walker tumor growth in partially hepatectomized rats
AUTHOR(S): Gershbein, Leon L.
CORPORATE SOURCE: Northwest Inst. for Med. Res., Chicago
SOURCE: Cancer Research (1966), 26(9;Pt. 1), 1905-8
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The restoration of liver weight in subtotally hepatectomized rats with Walker tumor cells transplanted into the caudal lobe of the remaining liver, was stimulated by feeding diets supplemented with coramine, butazolidine, 2,4-dithiopyrimidine, thalidomide, and acenaphthene, or by subcutaneous injections of acenaphthene, or 9,10-dimethyl-1,2- benzanthracene. Thiouracil, disulfiram, and usnic acid gave rise to liver weight increments which were in the range of their resp. controls. Dietary supplements of nicotinamide, cycloleucine, D-Lethionine, and 6-mercaptopurine, or a subcutaneous injection of cortisone acetate decreased the liver weight gain to levels below that of their resp. controls. The mean wet tumor wts. were not affected by any of these drugs, except by nicotinamide, which elicited a decrease in tumor weight 18 references.

L5 ANSWER 50 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:108243 CAPLUS Full-text
DOCUMENT NUMBER: 64:108243
ORIGINAL REFERENCE NO.: 64:20446a-c
TITLE: Thalidomide and tumor
AUTHOR(S): Mueckter, H.; More, E.
CORPORATE SOURCE: Chem. Gruenenthal G.m.b.H. Stolberg-Rheinland, Germany
SOURCE: Arzneimittel-Forschung (1966), 16(2), 129-34
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The addition of 1% thalidomide to the diet of rats 2 days before intubation of 20 mg. 7,12-dimethylbenz[α]anthracene (DMBA) delayed both the appearance and growth of DMBA-induced tumors. In rats already infected with DMBA-induced tumors, 1% thalidomide also limited the manifestation and, to a certain extent, growth of the tumors. The curative effect was limited by the size of the tumors at the time of 1st application and by the duration of treatment. Thalidomide had no significant effect on the spontaneously developing, hormone-independent mammary cancer induced by the milk factor virus in C3H/O20 mice. The mechanism of antitumor action of thalidomide differed from the cytostatic action of cyclophosphamide in that thalidomide seemed to exert its effect mainly, or perhaps exclusively, through the endocrine system.

L5 ANSWER 51 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:30357 CAPLUS Full-text
DOCUMENT NUMBER: 64:30357
ORIGINAL REFERENCE NO.: 64:5658d-f
TITLE: Biochemical effects of thalidomide and a histogenetic hypothesis of the malformation of the fetus
AUTHOR(S): Nystrom, Cl.
CORPORATE SOURCE: Univ. Sahlgrenska Sjukhuset, Goteborg, Swed.
SOURCE: Intern. Congr. Chemotherapy, Proc., 3rd, Stuttgart (1964), 1963(1), 372-8
DOCUMENT TYPE: Journal
LANGUAGE: English

AB cf. CA 59, 4441g. Since thalidomide (I) has an N-phthaloylglutamic acid imide structure its possible actions as an antimetabolite against folic acid (II) was investigated. Over 1-3 months, I was administered by injection and orally to 2 patients with tetratoid carcinomas of an embryonal type, presumably with enzyme patterns like that of a fetus. One was a woman of 25 years with an ovarian cancer, the other was a man of 42 with carcinoma of the testes. Blood levels of II were little affected by I. However, I had some effect as an antagonist to II. In doses higher than 3 g./day (as high as 7 g./day), I appeared to interfere with II metabolism as indicated by increased amts. of urinary formiminoglutamic acid. In growth inhibition tests, I did not affect the growth of Streptococcus faecalis or Lactobacillus casei. Hence I did not act as a II antagonist in bacterial growth. For the in vivo human tests, there was an uptake of I by tumor tissue but no particularly marked effects of I on tumor growth. This may perhaps have resulted from the fact that the tumors and their metastases had been treated with heavy doses of ionizing radiations. However, the results suggested that II-dependent tumors might show pharmacotherapeutic responses to I or some of its metabolites. 13 references.

L5 ANSWER 52 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:30356 CAPLUS Full-text

DOCUMENT NUMBER: 64:30356
ORIGINAL REFERENCE NO.: 64:5658c-d
TITLE: Effects of cytostatic and tuberculostatic agents in patients with bronchial carcinoma plus active lung tuberculosis
AUTHOR(S): Hammer, O.
CORPORATE SOURCE: Hosp. Falkenstein, Germany
SOURCE: Intern. Congr. Chemotherapy, Proc., 3rd, Stuttgart (1964), 1963(1), 209-11
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The mechanisms of action of the title agents are discussed. In combined treatments, no undue side effects were observed, and no antagonism could be demonstrated between nitrogen mustard derivs. containing an active NCH2CH2 group and antitubercular drugs such as streptomycin or isoniazid. 23 references.

L5 ANSWER 53 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:14172 CAPLUS Full-text
DOCUMENT NUMBER: 64:14172
ORIGINAL REFERENCE NO.: 64:2634b-c
TITLE: Deformations by chemical substances. Experiments on rabbits furnish new results
AUTHOR(S): Gottschewski, Georg H. M.
SOURCE: Umschau Wiss. Tech. (1965), 65(7), 199-203
DOCUMENT TYPE: Journal
LANGUAGE: German

AB Cyclophosphamide (used for cancer treatment under the name of Endoxan and thalidomide (Contergan) have no effect on specific organs of the fetus. Their effect depends on the time they are administered; it is more pronounced at an early stage because then organs are not yet differentiated and are concentrated in a small area. At later stages of development, however, deformations of individual organs can be produced.

L5 ANSWER 54 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:474983 CAPLUS Full-text
DOCUMENT NUMBER: 63:74983
ORIGINAL REFERENCE NO.: 63:13855f-g
TITLE: Side effects of anabolic steroids
AUTHOR(S): Suzuki, Hidero; Ogata, Etsuro
CORPORATE SOURCE: Univ. Tokyo
SOURCE: Sogo Igaku (1963), 20, 431-5
CODEN: SOIGAG; ISSN: 0371-1803
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB A review with 15 references.

L5 ANSWER 55 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:39524 CAPLUS Full-text
DOCUMENT NUMBER: 62:39524
ORIGINAL REFERENCE NO.: 62:6997c-d
TITLE: Antitumor activity of thalidomide
AUTHOR(S): Gaetani, M.
CORPORATE SOURCE: Ist. Nazl. Studio Tumori, Milan
SOURCE: Giorn. Ital. Chemioterap. (1964), 11(2), 83-6
DOCUMENT TYPE: Journal
LANGUAGE: Italian

AB Daily administration of 500 mg. thalidomide/kg. (I) to tumor -inoculated mice for 14 days had no influence on the normal development of the following tumors: Ehrlich ascites tumor, myeloma Oberling-Guerin-Guerin, sarcoma 180, and transplantable teratoma. This proved to be so for both racemic I and for the pure L(-)-isomer. The body weight and mortality of the mice were not affected by the latter 2 compds.

L5 ANSWER 56 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:464521 CAPLUS Full-text
DOCUMENT NUMBER: 61:64521
ORIGINAL REFERENCE NO.: 61:11213d-h
TITLE: Influence of anticancer agents on the metabolism of δ-aminolevulinic acid in normal and tumor-bearing mice
AUTHOR(S): Hano, Kotobuki; Akashi, Akira
CORPORATE SOURCE: Univ. Osaka, Japan
SOURCE: Gann (1964), 55(1), 25-40
CODEN: GANNA2; ISSN: 0016-450X
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Previous findings had shown that the effect of anticancer agents in restoring lowered enzyme activities in the liver, especially that of catalase, was not always in parallel with their therapeutic effect. To clarify this, the possible inhibitory effect of these agents on heme metabolism, with special reference to Fe, Cu, and δ-aminolevulinic acid (I) metabolism, was investigated in normal and tumor-bearing mice. I dehydratase activity in the liver of tumor bearers was lower than that of normal animals and was very low in tumor cells. Of the anticancer agents tested in vitro, 2,5-bis(ethylenimino)-1,4- benzoquinone and folic acid antagonists inhibited this enzyme in normal mice. On the other hand, carboxamide utilization, in which I is involved with the source of a C1 fragment, occurred at a much higher rate in tumor cells than in the livers of normal and tumor -bearing mice. In the presence of folic acid antagonists, d-catechol, and berberine, carboxamide utilization by tumor cells was markedly inhibited in vitro. Daily decrease in the serum Fe level, blood hemoglobin content, and liver I dehydratase activity was observed after tumor transplantation, at which time serum Cu level increased. Administration of alkylating agents and 8-azaguanine to tumor bearers restored these metabolic disturbances to normal in parallel with their therapeutic effects. These agents showed no influence on these levels in normal mice. 6-Mercaptopurine, which has a marked anticancer activity with Ehrlich ascites carcinoma, returned the lower liver I dehydratase activity and elevated serum Cu level in tumor -bearing animals to normal. However, the lowered serum Fe level and blood hemoglobin content in tumor bearers were further depressed by treatment with 6-mercaptopurine, and this depressive action was also found in normal mice. Treatment with aminopterin, which was not effective against Ehrlich ascites carcinoma, did not restore the altered metabolism of tumor-bearing animals to normal, and it caused a depression of the blood hemoglobin content in normal mice.

L5 ANSWER 57 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:457061 CAPLUS Full-text
DOCUMENT NUMBER: 61:57061
ORIGINAL REFERENCE NO.: 61:9922a-b
TITLE: Thalidomide; effects on Ehrlich ascites tumor cells in vitro
AUTHOR(S): DiPaolo, Joseph A.; Wenner, Charles E.
CORPORATE SOURCE: Roswell Park Mem. Inst., Buffalo, NY
SOURCE: Science (Washington, DC, United States) (1964),

144(3626), 1583
CODEN: SCIEAS; ISSN: 0036-8075
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Thalidomide did not inhibit dehydrogenase activity or growth of Ehrlich ascites tumor cells; it increased the mitotic activity in vitro, but did not affect O uptake. The effect of thalidomide was not altered by the addition of nicotinic or folic acids, or by vitamin B1 or B6.

L5 ANSWER 58 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:406964 CAPLUS Full-text
DOCUMENT NUMBER: 61:6964
ORIGINAL REFERENCE NO.: 61:1130f
TITLE: The possible antineoplastic effect of thalidomide
AUTHOR(S): Bach, A.; Bichel, J.; Hejgaard, J. J.
CORPORATE SOURCE: Union Aarhus, Den.
SOURCE: Acta Pathologica et Microbiologica Scandinavica (1963), 59(4), 491-9
CODEN: APMIAL; ISSN: 0365-5555
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mice were relatively insensitive to thalidomide, and even doses many times larger than those which are definitely hypnotic in man did not produce any visible sedative effect. Amts. 1000 times as high as the hypnotic dose/kg. body weight in man induced sleep for some hours in the animals, which could, however, always easily be aroused. Very large doses of thalidomide did not show any inhibitory effect on NJA, PBH, and GH tumor growth in C3H mice.

L5 ANSWER 59 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:63728 CAPLUS Full-text
DOCUMENT NUMBER: 60:63728
ORIGINAL REFERENCE NO.: 60:11245c-d
TITLE: In vitro test systems for cancer therapy. II. Correlation of in vitro inhibition of dehydrogenase and growth with in vivo inhibition of Ehrlich ascites tumor
AUTHOR(S): DiPaolo, Joseph A.
CORPORATE SOURCE: Roswell Park Mem. Inst., Buffalo, NY
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1963), 114, 384-7
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. Cancer Res. 23, 184-90(1963). Fifteen diverse chemotherapeutic compds. of clin. value as well as those of wide effectiveness in animal tumor systems are shown to give varying responses in vitro. The extent of inhibition by any one compound in vitro ranges from none to significant, depending on the exact in vitro conditions. The dehydrogenase enzyme inhibition test was the most successful on the basis of correlation with extension of survival time of mice bearing the same tumor used in the in vitro studies.

L5 ANSWER 60 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:55507 CAPLUS Full-text
DOCUMENT NUMBER: 60:55507
ORIGINAL REFERENCE NO.: 60:9792g-h,9793a
TITLE: Thalidomide-induced alterations in the blastocyst and placenta and the armadillo, Dasypus novemcinctus

mexicanus, including a choriocarcinoma
AUTHOR(S): Marin-Padilla, Miguel; Benirschke, Kurt
CORPORATE SOURCE: Dartmouth Med. School, Hanover, NH
SOURCE: American Journal of Pathology (1963), 43(6), 999-1016
CODEN: AJPAA4; ISSN: 0002-9440
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Thalidomide was fed to pregnant armadillos for several days in daily doses of 100 mg./kg. All animals became ill, a majority aborted or failed to implant. Degenerative changes were observed in blastocytes and the trophoblastic columns in the developing placentas. The alterations appeared to have led to fetal bleeding and hematopoietic response. In 1 animal treated during earliest implantation stages an embryo showed asym. phocomelia. This animal developed a widely metastatic choriocarcinoma from the placenta. Embryoid bodies were found in the metastases of the tumor, and endocrine response suggested the presence of chorionic gonadotropin. Only one litter with malformations similar to those seen in man and some exptl. animals was produced. The reason for this failure was presumably the degree of toxicity resulting in abortions in the first exptl. group and the difficulty in exact timing of the pregnancies. While the dose given exceeded the teratogenic dose reported for man, it was apparent that thalidomide had considerable effect in this species. Its sensitivity to the drug apparently was greater than that of other exptl. animals.

L5 ANSWER 61 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:465105 CAPLUS Full-text
DOCUMENT NUMBER: 59:65105
ORIGINAL REFERENCE NO.: 59:12051a-b
TITLE: Inhibitory effect of antiviral compounds on viruses in vivo and in mouse ascites cells in vitro
AUTHOR(S): Furusawa, Eiichi; Cutting, Windsor; Furst, Arthur
CORPORATE SOURCE: Stanford Univ., Stanford, CA
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1963), 112, 617-22
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Antiviral activities of a number of known antiviral compds., including 2-(αhydroxybenzyl)benzimidazole, 5-iodo-2'-deoxyuridine, fluoro- phenylalanine, N-methylisatin thiosemicarbazone, (NH4)2SO4, Statolon, and Helenine, on Columbia SK and LCM virus propagation in cultures of mouse ascites tumor cells are described. These compds. were also compared with some other compds. not previously recognized as antiviral: methylglyoxal bisguanylhydrazone, 1,6-dinitronaphthalene, the dihexachlorocyclopentadiene adduct of 2-carboxy-3-naphthalenesulfonic acid, phosphotungstic acid, and vitamin B12. Statolon was effective against Columbia SK infection when given prophylactically 2 days before inoculation of the virus.

L5 ANSWER 62 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:465080 CAPLUS Full-text
DOCUMENT NUMBER: 59:65080
ORIGINAL REFERENCE NO.: 59:12046h,12047a
TITLE: Tumor-inhibiting compounds in the group of 9-aminoacridine derivatives
AUTHOR(S): Ledochowski, Z.; Ledochowski, A.; Radzikowski, C.
CORPORATE SOURCE: Politech., Danzig, Pol.
SOURCE: Bulletin de l'Academie Polonaise des Sciences, Serie des Sciences Chimiques (1961), 9, 179-82

CODEN: BAPCAQ; ISSN: 0001-4095
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A total of 49 derivs. of 9-aminoacridine, 27 derivs. of N-phenylanthranilic acid, and 21 derivs. of 9-chloroacridine were prepared and investigated as to their tumor-inhibiting activity on mice with Crocker sarcoma. A correlation existed between the structure of the examined compds. and their tumor-inhibiting activity. Of the 6 compds. which proved to be active, 5 were derivs. of N,N- dimethylputrescine and only one a derivative of N,N-dimethyl-1,3- diaminopropane; the derivs. containing other amines in position 9 were inactive. The activity is usually suppressed by the substitution of Cl for Br in position 1 or 3, H for Br, and Et for the Me group at the terminal N of the side chain.

L5 ANSWER 63 OF 63 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:424400 CAPLUS Full-text
DOCUMENT NUMBER: 59:24400
ORIGINAL REFERENCE NO.: 59:4441g-h,4442a
TITLE: Biochemical effects of thalidomide
AUTHOR(S): Nystrom, C.
CORPORATE SOURCE: Radiotherapy Centre, Goteborg, Swed.
SOURCE: Scandinavian Journal of Clinical and Laboratory Investigation (1963), 15, 102-3
CODEN: SJCLAY; ISSN: 0036-5513
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Because the chemical structure of thalidomide is related to that of folic acid, there is an enzymic interaction at the one-C-stage. A blocked folio acid action leads to urinary excretion of the intermediary formiminoglutamic acid (I). The amount of I excreted may be regarded as a measure of folic acid antagonism. In vitro microbiol. growth inhibition tests with Lactobacillus easel and Streptococcus faecalis show no folic acid antagonism by thalidomide. Treatment of 2 patients with therapy-resistant teratoid carcinomas in advanced stages showed normal I tests when the daily dose of thalidomide was below 3 g. Doses of 3-7 g. daily showed a marked increase in urinary excretion of I proportional to the dosage. Analysis of tumor tissue revealed thalidomide uptake. It is concluded that folic acid-dependent embryological tumors may be susceptible to thalidomide, and that embryonic germinative epithelium having a high folic acid requirement is deprived of its needs by the biochem. action of thalidomide.

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     (FILE 'HOME' ENTERED AT 15:35:25 ON 26 JUL 2007)

     FILE 'REGISTRY' ENTERED AT 15:36:20 ON 26 JUL 2007
               E "THALIDOMIDE"/CN 25
L1             1 S E3

     FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 15:37:30 ON 26 JUL
     2007
L2          6948 S L1
L3          2153 S L2 AND (CANCER OR TUMOR OR TUMOROGENESIS)
L4           109 S L3 NOT PY>1995
L5            63 S L4 NOT PY>1993
L6             0 S L5 AND ANGIOGENESIS
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L7              6 S L5 AND "TUMOR GROWTH"
L8             53 S L5 AND "TUMOR"

=> s 15 and human
L9             10 L5 AND HUMAN

=> d 19 1-10 ibib ,abs

L9   ANSWER 1 OF 10      MEDLINE on STN
ACCESSION NUMBER:    93317606      MEDLINE  Full-text
DOCUMENT NUMBER:     PubMed ID: 8327469
TITLE:               Thalidomide inhibits the replication of human
                     immunodeficiency virus type 1.
AUTHOR:              Makonkawkeyoon S; Limson-Pobre R N; Moreira A L; Schauf V;
                     Kaplan G
CORPORATE SOURCE:    Rockefeller University, New York, NY 10021.
CONTRACT NUMBER:     AI-22616 (NIAID)
                     AI-24775 (NIAID)
SOURCE:              Proceedings of the National Academy of Sciences of the
                     United States of America, (1993 Jul 1) Vol. 90, No. 13, pp.
                     5974-8.
                     Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
                     (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals; AIDS
ENTRY MONTH:         199308
ENTRY DATE:          Entered STN: 20 Aug 1993
                     Last Updated on STN: 3 Feb 1997
                     Entered Medline: 6 Aug 1993
AB   Thalidomide, a selective inhibitor of tumor necrosis factor alpha (TNF-alpha)
     synthesis, suppresses the activation of latent human immunodeficiency virus
     type 1 (HIV-1) in a monocytoid (U1) line. The inhibition is dose dependent
     and occurs after exposure of the cells to recombinant TNF-alpha, phorbol
     myristate acetate, lipopolysaccharide, and other cytokine combinations.
     Associated with HIV-1 inhibition is a reduction in agonist-induced TNF-alpha
     protein and mRNA production. Thalidomide inhibition of virus replication in
     the phorbol myristate acetate- and recombinant TNF-alpha-stimulated T-cell
     line ACH-2 is not observed. The presence of thalidomide also inhibits the
     activation of virus in the peripheral blood mononuclear cells of 16 out of 17
     patients with advanced HIV-1 infection and AIDS. These results suggest the
     use of thalidomide in a clinical setting to inhibit both virus replication and
     the TNF-alpha-induced systemic toxicity of HIV-1 and opportunistic infections.

L9   ANSWER 2 OF 10      MEDLINE on STN
ACCESSION NUMBER:    93103729      MEDLINE  Full-text
DOCUMENT NUMBER:     PubMed ID: 1466907
TITLE:               Effect of blocking TNF-alpha on intracellular BCG (Bacillus
                     Calmette Guerin) growth in human monocyte-derived
                     macrophages.
AUTHOR:              Fazal N; Lammas D A; Raykundalia C; Bartlett R; Kumararatne
                     D S
CORPORATE SOURCE:    Department of Immunology, University of Birmingham, UK.
SOURCE:              FEMS microbiology immunology, (1992 Dec) Vol. 5, No. 5-6,
                     pp. 337-45.
                     Journal code: 8901230. ISSN: 0920-8534.
PUB. COUNTRY:        Netherlands
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DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199301
ENTRY DATE: Entered STN: 12 Feb 1993
Last Updated on STN: 12 Feb 1993
Entered Medline: 25 Jan 1993

AB Four agents, thalidomide, oxpentifylline, dexamethasone and a polyclonal anti-TNF-alpha antibody, were all shown by specific Elisa to block endogenous TNF-alpha production by Bacillus Calmette Guerin (BCG)-infected human monocyte-derived macrophages in in vitro culture. There was however no significant enhancement of intracellular BCG growth, over a 7-day incubation, in human monocyte-derived macrophages in the presence of any of the TNF-alpha-blocking agents, as determined by both radiometric and CFU counting methods of assessing bacterial viability and growth. The result suggests that the action of TNF-alpha alone is unlikely to be an important effector mechanism in antimycobacterial immunity within human cells.

L9 ANSWER 3 OF 10 MEDLINE on STN
ACCESSION NUMBER: 91203215 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2016904
TITLE: Induction of morphological differentiation in the human leukemic cell line K562 by exposure to thalidomide metabolites.
AUTHOR: Hatfill S J; Fester E D; de Beer D P; Bohm L
CORPORATE SOURCE: Radiotherapy Department, Faculty of Medicine, University of Stellenbosch, Tygerberg, R.S.A.
SOURCE: Leukemia research, (1991) Vol. 15, No. 2-3, pp. 129-36.
Journal code: 7706787. ISSN: 0145-2126.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 7 Jun 1991
Last Updated on STN: 3 Feb 1997
Entered Medline: 17 May 1991

AB The lineage and state of differentiation of cells in the mammalian haemopoietic compartment is associated with specific patterns of homeobox gene expression (EMBO J. 7, 2131, 1988). Agents which influence homeobox gene expression are thus of great interest in the study of human leukemias. Retinoic acid has direct regulatory actions on homeobox gene transcription (TIBS 158, 52, 1989; Differentiation 37, 773, 1988) and can induce select human leukemia cell lines to undergo terminal differentiation in vitro (Proc. natl Acad. Sci. U.S.A. 77, 2936, 1980). Retinoic acid is also a known teratogen for vertebrate foetal limb-bud development. Some of the teratogenic effects are duplicated by the drug Thalidomide (Embryopathic Activity of Drugs, Little Brown, Boston, p. 167, 1965; Haematological Cytology, Wolf Med. Pub. Ltd, London, p. 118, 1982). To investigate Thalidomide for other retinoid-like effects, we exposed cultures of human leukemia K562 cells to the metabolites generated in a Thalidomide hepatic-microsomal enzyme drug metabolizing system (Proc. natl Acad. Sci. U.S.A. 78, 2545, 1981). Here we report evidence that a single 2 h pulse-exposure to Thalidomide metabolites, induces K562 cells to undergo morphological differentiation in vitro. We also demonstrate a significant cytotoxic effect for these metabolites.

L9 ANSWER 4 OF 10 MEDLINE on STN
ACCESSION NUMBER: 91147899 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1997652
TITLE: Thalidomide selectively inhibits tumor necrosis factor alpha production by stimulated human monocytes.
AUTHOR: Sampaio E P; Sarno E N; Galilly R; Cohn Z A; Kaplan G
CORPORATE SOURCE: Laboratory of Cellular Physiology and Immunology, Rockefeller University, New York, New York 10021.
CONTRACT NUMBER: AI-22616 (NIAID)
SOURCE: The Journal of experimental medicine, (1991 Mar 1) Vol. 173, No. 3, pp. 699-703.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199104
ENTRY DATE: Entered STN: 19 Apr 1991
Last Updated on STN: 3 Feb 1997
Entered Medline: 2 Apr 1991

AB Thalidomide selectively inhibits the production of human monocyte tumor necrosis factor alpha (TNF-alpha) when these cells are triggered with lipopolysaccharide and other agonists in culture. 40% inhibition occurs at the clinically achievable dose of the drug of 1 micrograms/ml. In contrast, the amount of total protein and individual proteins labeled with [35S]methionine and expressed on SDS-PAGE are not influenced. The amounts of interleukin 1 beta (IL-1 beta), IL-6, and granulocyte/macrophage colony-stimulating factor produced by monocytes remain unaltered. The selectivity of this drug may be useful in determining the role of TNF-alpha in vivo and modulating its toxic effects in a clinical setting.

L9 ANSWER 5 OF 10 MEDLINE on STN
ACCESSION NUMBER: 75070562 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 4140679
TITLE: Human experiences related to adverse drug reactions to the fetus or neonate from some maternally administered drugs.
AUTHOR: Shirkey H C
SOURCE: Advances in experimental medicine and biology, (1972) Vol. 27, pp. 17-30.
Journal code: 0121103. ISSN: 0065-2598.
Report No.: PIP-723949; POP-00015296.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 197503
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 1 Nov 2002
Entered Medline: 17 Mar 1975

AB This is a review of known periods in utero during which drugs alter the process of growth; effects may be shown on the fetus or the newborn and vary with the stage of development of the fetus when exposed. Other variables are the mother and the placenta. There is no safe animal screening mechanism, the human test is by ordeal, and more clinical monitoring and reporting are

needed. Cancer chemotherapeutic agents exert their maximal effects on rapidly dividing cells and are therefore hazardous during pregnancy; the greatest risk is in the 1st trimester. In the thalidomide experience the critical days were the 22nd and 23rd days after conception. Masculinizing drugs such as testosterone and other androgenic steroids have been implicated as affecting the female fetus when given early in pregnancy. Oral contraceptives taken by an already pregnant woman are a hazard because of these progestational agents. Progesterone alone is unlikely to cause masculinization but other progestins may cause such changes. Carcinogenesis may develop later in females born of mothers who are treated with diethylstilbestrol to prevent miscarriage. Many antithyroid drugs have caused neonatal goiter. Maternal ingestion of iodides during pregnancy (preparations for treating asthma, cough syrups, radio-contrast media used in diagnoses) is the most frequent cause. Goiter is relatively common in infants whose mothers were treated with propylthiouracil and other antithyroid drugs, yet they usually show normal thyroid function. However, hypothyroidism with cretinism can occur. Lithium, used in psychiatry and as a salt substitute, may alter iodine metabolism and thyroid gland function. It also passes into the milk to continue the potential toxicity. Teratogenic effects in experimental animals suggest other possible effects on infants from lithium and similar drugs.

L9 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:508464 CAPLUS Full-text
DOCUMENT NUMBER: 119:108464
TITLE: Thalidomide inhibits the replication of human immunodeficiency virus type 1
AUTHOR(S): Makonkawkeyoon, Sanit; Limson-Pobre, Rhona N. R.; Moreira, Andre L.; Schauf, Victoria; Kaplan, Gilla
CORPORATE SOURCE: Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1993), 90(13), 5974-8
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Thalidomide, a selective inhibitor of tumor necrosis factor α (TNF-α) synthesis, suppresses the activation of latent human immunodeficiency virus type 1 (HIV-1) in a monocytoid (U1) line. The inhibition is dose dependent and occurs after exposure of the cells to recombinant TNF-α, phorbol myristate acetate, lipopolysaccharide, and other cytokine combinations. Associated with HIV-1 inhibition is a reduction in agonist-induced TNF-α protein and mRNA production Thalidomide inhibition of virus replication in the phorbol myristate acetate- and recombinant TNF-α-stimulated T-cell line ACH-2 is not observed The presence of thalidomide also inhibits the activation of virus in the peripheral blood mononuclear cells of 16 out of 17 patients with advanced HIV-1 infection and AIDS. These results suggest the use of thalidomide in a clin. setting to inhibit both virus replication and the TNF-α-induced systemic toxicity of HIV-1 and opportunistic infections.

L9 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:156793 CAPLUS Full-text
DOCUMENT NUMBER: 114:156793
TITLE: Thalidomide selectively inhibits tumor necrosis factor α production by stimulated human monocytes
AUTHOR(S): Sampaio, Elizabeth P.; Sarno, Euzenir N.; Galilly, Ruth; Cohn, Zanvil A.; Kaplan, Gilla
CORPORATE SOURCE: Lab. Cell. Physiol. Immunol., Rockefeller Univ., New

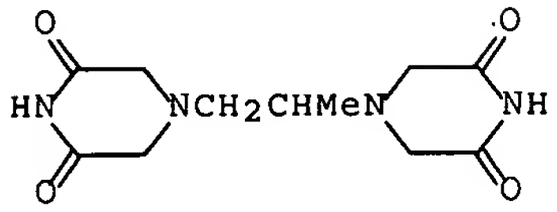
York, NY, 10021, USA
SOURCE: Journal of Experimental Medicine (1991), 173(3), 699-703
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Thalidomide selectively inhibits the production of human monocyte tumor necrosis factor-α (TNF-α) when these cells are triggered with lipopolysaccharide and other agonists in culture. A 40% inhibition occurs at the clin. achievable concentration of 1 μg/mL. The amount of total protein and individual proteins labeled with [35S]methionine detected by SDS-PAGE are not affected by thalidomide. The amts. of interleukin 1β (IL-1β), IL-6, and granulocyte/macrophage colony-stimulating factor produced by monocytes remain unaltered. The selectivity of this drug may be useful in determining the role of TNF-α in vivo and modulating its toxic effects in a clin. setting.

L9 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:52389 CAPLUS Full-text
DOCUMENT NUMBER: 110:52389
TITLE: Evaluation of two in vitro assays to screen for potential developmental toxicants
AUTHOR(S): Steele, Vernon E.; Morrissey, Richard E.; Elmore, Eugene L.; Gurganus-Rocha, Deborah; Wilkinson, Betty P.; Curren, Rodger D.; Schmetter, Barry S.; Louie, Audrey T.; Lamb, James C., IV; Yang, Li L.
CORPORATE SOURCE: Northrop Services, Inc., Research Triangle Park, NC, 27709, USA
SOURCE: Fundamental and Applied Toxicology (1988), 11(4), 673-84
CODEN: FAATDF; ISSN: 0272-0590
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To evaluate two in vitro assays for their ability to detect known developmental toxicants and nontoxicants, a series of 44 coded compds. were assayed by 2 independent labs. using standardized protocols. The 2 test systems were the human embryonic palatal mesenchymal cell growth inhibition assay and the mouse ovarian tumor cell attachment inhibition assay. After all compds. were tested, they were decoded and ranked according to the min. IC50 value (the millimolar concentration of compound which inhibits growth or attachment by 50% compared to the solvent control) from either test. The in vitro test result concordance with established in vivo animal and human test results was examined over a wide range of concentration levels (above which the in vitro results were called pos. and below which they were considered neg.). A pos. response from either test was defined as a pos. in vitro response. Concordance was defined as the number of correct responses divided by the number of chems. tested. At the 1-mM level, the concordance of data from the combined in vitro assays with the in vivo data was 66% in one laboratory and 58% in the other. The maximum agreement between the combined in vitro and in vivo data was reached at the 20-mM level, where there was a 73 and 74% concordance of results in the 2 labs. At that level, there was a 16 and 10% incidence of false neg. results, and a 54 and 77% incidence of false pos. results. A portion of these false neg. compds. may require metabolic activation. The use of either assay alone was not as accurate as using a pos. result from either test. Agreement of the in vitro data at the 10-mM level with available human data was 71 and 75% for each laboratory Thus, 2 assays are complimentary and the combination of these assays could be useful as a preliminary screen to establish priorities for in vivo developmental toxicity testing.

L9 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:537359 CAPLUS Full-text
DOCUMENT NUMBER: 85:137359
TITLE: Factors related to tumor spread in the body
AUTHOR(S): Boggust, W. A.
CORPORATE SOURCE: Dep. Exp. Med., Trinity Coll., Dublin, Ire.
SOURCE: Advances in Tumour Prevention, Detection and Characterization (1976), 3(Biol. Charact. Hum. Tumours, Proc. Int. Symp., 6th, 1975), 383-90
CODEN: APDCDT
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



II

AB In exts. of human cancers, cathepsins B, C, and D, leucine aminopeptidase [9001-61-0], glucosaminidase [9027-56-9], acid and neutral collagenase [9001-12-1], and fibrinolysin [9001-90-5] activities were found. Collagenase was blocked by the chelating agents dimercaptopropanol (BAL) [59-52-9], EDTA [60-00-4], and o-phenanthroline (I) [66-71-7], and the cytostatic drug ICRF-159 (II) [21416-87-5]. Combinations of I and II were synergistic. II also inhibited cathepsins C and B1 and probably glucosaminidase, but not cathepsin D or leucineaminopeptidase. Mice bearing implanted carcinoma excised on the 10th day, died from lung metastases within 34 days unless otherwise treated. Survival periods were increased by II, but not by I alone. Combinations of I and II substantially increased the survival period. Thus, I and II by acting as enzyme inhibitors and cytotoxic agents they helped to inhibit primary tumor growth and prevent metastases.

L9 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:30357 CAPLUS Full-text
DOCUMENT NUMBER: 64:30357
ORIGINAL REFERENCE NO.: 64:5658d-f
TITLE: Biochemical effects of thalidomide and a histogenetic hypothesis of the malformation of the fetus
AUTHOR(S): Nystrom, Cl.
CORPORATE SOURCE: Univ. Sahlgrenska Sjukhuset, Goteborg, Swed.
SOURCE: Intern. Congr. Chemotherapy, Proc., 3rd, Stuttgart (1964), 1963(1), 372-8
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. CA 59, 4441g. Since thalidomide (I) has an N-phthaloylglutamic acid imide structure its possible actions as an antimetabolite against folic acid (II) was investigated. Over 1-3 months, I was administered by injection and orally to 2 patients with tetratoid carcinomas of an embryonal type, presumably with enzyme patterns like that of a fetus. One was a woman of 25 years with an ovarian cancer, the other was a man of 42 with carcinoma of the testes. Blood

levels of II were little affected by I. However, I had some effect as an antagonist to II. In doses higher than 3 g./day (as high as 7 g./day), I appeared to interfere with II metabolism as indicated by increased amts. of urinary formiminoglutamic acid. In growth inhibition tests, I did not affect the growth of Streptococcus faecalis or Lactobacillus casei. Hence I did not act as a II antagonist in bacterial growth. For the in vivo human tests, there was an uptake of I by tumor tissue but no particularly marked effects of I on tumor growth. This may perhaps have resulted from the fact that the tumors and their metastases had been treated with heavy doses of ionizing radiations. However, the results suggested that II-dependent tumors might show pharmacotherapeutic responses to I or some of its metabolites. 13 references.

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(FILE 'HOME' ENTERED AT 15:35:25 ON 26 JUL 2007)

FILE 'REGISTRY' ENTERED AT 15:36:20 ON 26 JUL 2007
E "THALIDOMIDE"/CN 25
L1 1 S E3

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 15:37:30 ON 26 JUL 2007
L2 6948 S L1
L3 2153 S L2 AND (CANCER OR TUMOR OR TUMOROGENESIS)
L4 109 S L3 NOT PY>1995
L5 63 S L4 NOT PY>1993
L6 0 S L5 AND ANGIOGENESIS
L7 6 S L5 AND "TUMOR GROWTH"
L8 53 S L5 AND "TUMOR"
L9 10 S L5 AND HUMAN

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	204.89	213.11
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-33.54	-33.54

STN INTERNATIONAL LOGOFF AT 15:52:12 ON 26 JUL 2007